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(54) Title: GENETIC SEQUENCES CONFERRING DISEASE RESISTANCE IN PLANTS AND USES THEREFOR

(57) Abstract

The present invention relates generally to genetic sequences, and more particularly to genetic sequences which confer or otherwise facilitate disease resistance in plants such as against rust and mildew. The present invention further provides for transgenic plants carrying the subject genetic sequences enabling the generation of disease resistant plants. The present invention is particularly useful for developing disease resistance in crop varieties.

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GENETIC SEQUENCES CONFERRING DISEASE RESISTANCE IN PLANTS AND USES THEREFOR

The present invention relates generally to genetic sequences, and more particularly to genetic sequences which confer or otherwise facilitate disease resistance in plants such as against rust and mildew. The present invention further provides for transgenic plants carrying the subject genetic sequences enabling the generation of disease resistant plants. The present invention is particularly useful for developing disease resistance in crop varieties.

Bibliographic details of the publications numerically referred to in this specification are collected at the end of the description. Sequence Identity Numbers (SEQ ID NOs.) for the nucleotide and amino acid sequences referred to in the specification are defined following the bibliography.

Throughout this specification, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element or integer or group of elements or integers but not the exclusion of any other element or integer or group of elements or integers.

The rapidly increasing sophistication of recombinant DNA technology is greatly facilitating the efficacy of commercially important agricultural processes. Of particular concern is the effect of plant diseases on the efficacy of these agricultural processes. Plant diseases and particularly diseases in crop plants represent a major contributing factor in crop losses capable of causing economically significant down turn in productivity per square metre. The development, therefore, of disease resistant plants is an important goal in agricultural and horticultural research.

Major genes conditioning resistance to plant diseases have been investigated extensively in agriculture. Of particular economic importance are genes controlling resistance to rust and mildew. Rust is an especially significant problem amongst broad acre crops such as wheat, barley and cereal grains and is caused by infection with a class of fungi known as the *Basidiomycetes*. Although rust resistance genes are a potentially invaluable genetic resource in agriculture, the molecular basis of major gene resistance is unknown and, until the present invention, genes conferring rust or mildew resistance had not been cloned.

Genetic analysis indicates that rust resistance genes control specific recognition of the products of rust avirulence genes. In developing disease resistance varieties using disease resistance genes, plant breeders deploy resistance genes that match the avirulence genes present in the local strains of the pathogens. The pathogen populations are dynamic and frequently new pathogenic strains arise by any number of means such as by mutation, recombination or accidental or natural introduction of new pathogenic strains. The existing disease resistant varieties then become susceptible to the new pathogenic strains. Plant breeders are then forced to develop new disease resistant varieties. At present, breeders use resistance genes that exist in either wheat or its relatives as their pool of new genes.

The cloning of a resistance gene is the first step in understanding the basis of resistance gene action and in particular the specificity control mechanism. Ellis *et al* (1) have described the development of a transposon tagging system to isolate rust resistance genes from flax (linseed, *Linum usitatissimum*). However, despite the general effectiveness of the methodology, the isolation of mutant flax plants possessing a tagged resistance gene has not been a straight forward procedure (2).

In accordance with the present invention, genetic sequences conferring rust resistance have been cloned from flax. The cloning of these sequences provides the means of generating transgenic plants with *de novo*, increased or otherwise enhanced rust resistance. The present invention also permits the screening through genetic or

immunological means similar rust resistance genes in other plants for use in developing or enhancing rust resistance in commercially and economically important species. Furthermore, the application of knowledge of the molecular basis behind resistance gene action and the specificity thereof offers the potential of a new source of genes produced by a variety of recombinant techniques. These new genes with altered disease resistance specificites are referred to herein as "modular resistance genes".

Accordingly, one aspect of the present invention comprises an isolated nucleic acid molecule comprising a sequence of nucleotides which confers or otherwise facilitates disease resistance in a plant. More particularly, the disease resistance is rust resistance. The present invention extends, however, to resistance to obligate biotrophic pathogens including but not limited to fungi, viruses and nematodes.

Another aspect of the present invention is directed to a nucleic acid molecule which comprises a sequence of nucleotides corresponding or complementary to the nucleotide sequence set forth in Figure 1 (SEQ ID NO:1) or having at least 45% similarity to all or part thereof and wherein said nucleic acid molecule confers or otherwise facilitates rust resistance in a plant.

In a related aspect of the present invention there is provided a nucleic acid molecule which comprises a sequence of nucleotides encoding or complementary to a sequence of nucleotides encoding the amino acid sequence set forth in Figure 1 (SEQ ID NOs:2 to 5) or having at least 45% similarity to all or part thereof and wherein said nucleic acid molecule confers or otherwise facilitates rust resistance in a plant

Preferably, the percentage similarity to the sequence set forth in SEQ ID NO:1 or SEQ ID NOs:2 to 5 is at least 50%. Even more preferably, the percentage similarity is at least 60%. Still more preferably, the percentage similarity is at least 65%. Yet still more preferably, the percentage similarity is at least 80-90% including at least 91% or 93% or 95%.

For the purposes of nomenclature, the sequences in Figure 1 relate to the "L6" allele of the disease resistance gene L which controls host resistance to flax rust races that carry the corresponding avirulence gene AL6. However, the present invention extends to other alleles of the gene or alleles of the M gene. Accordingly, a related embodiment of the present invention contemplates a nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a peptide, polypeptide or protein wherein said peptide, polypeptide or protein is capable of interacting with an avirulence gene product on a flax rust. Generally, when the rust resistance gene is the L6 allele, the corresponding avirulence gene is AL6. A similar nomenclature applied to the other alleles of the L gene, for example, the L2 and L10 alleles. Their corresponding avirulence genes are AL2 and AL10, respectively.

A further aspect of the present invention contemplates a nucleic acid molecule which confers or otherwise facilitates rust resistance in a plant and which is capable of hybridising under at least low stringency conditions to the nucleic acid molecule defined in SEQ ID NO:1.

For the purposes of defining the level of stringency, reference can conveniently be made to Sambrook *et al* (3), which is herein incorporated by reference, where the washing steps at pages 9.52-9.57 are considered high stringency. A "low" stringency is defined herein as being in 0.1-0.5% w/v SDS at 37-45°C for 2-3 hours. Depending on the source and concentration of nucleic acid involved in the hybridisation, alternative conditions of stringency may be employed such as "medium" stringent conditions which are considered herein to be 0.25-0.5% w/v SDS at ≥45°C for 2-3 hours or "high" stringent conditions as disclosed by Sambrook *et al* (3).

Although not intending to limit the present invention to any one theory or mode of action, it is proposed that the genetic sequences of the present invention are necessary for specific recognition of the products of rust avirulence genes. Accordingly, the genetic sequences are useful in enhancing existing rust resistance genes, providing *de*

novo the required specific recognition of rust avirulence gene products or being introduced together with rust avirulence genes on, for example, a single genetic cassette. Accordingly, these aspects of the invention are covered by the expression "conferring or otherwise enhancing rust resistance" or other similar expression.

The present invention is particularly directed to resistance conferring or facilitating genetic sequences from flax plants and from its relative *Linum marginale*. However, the subject invention clearly contemplates other sources of rust resistance genes such as but not limited to other species of *Linum*, soybeans, sunflowers and cereals amongst other plants including wild varieties of wheat, barley and maize.

The genetic sequences conferring or otherwise facilitating rust resistance may correspond to the naturally occurring sequence or may differ by one or more nucleotide substitutions, deletions and/or additions. Accordingly, the present invention extends to rust resistance genes and any functional alleles mutants, derivatives, parts, fragments, homologues or analogues thereof or non-functional molecules but which are at least useful as, for example, genetic probes or in the generation of immunologically interactive recombinant molecules. The present invention further extends to the promoter region from the rust resistance genes such as from L6, L2 or L10. A preferred promoter is from L6. Such promoters may be useful in driving expression of transgenes.

Examples of alleles of the flax rust resistance gene L include, but are not limited to L6, L2 and L10 although all alleles of the L locus are encompassed by the present invention. The present invention also extends to alleles of the M locus.

The present invention further contemplates recombinant or synthetic rust resistance gene products, such as the products of the L6, L2 or L10 alleles of the L resistance gene. A particularly preferred recombinant or synthetic rust resistance gene product is from the L6 gene. The L6 protein has the following features; an amino terminal half containing a nucleotide binding site (NBS) consisting of several motifs including the P-loop and further downstream, a kinase-2 motif (14). In L6, the kinase-2

sequence is ILVVLDDVD (SEQ ID NO:13) and more generally, XXXXDDX where X=L,I,V,F (using single amino acid nomenclature defined below). The C-terminal half of the polypeptide is a leucine rich region consisting of approximately 17% leucine residues. Within this region, stretches of residues appear where leucine is reiterated LXXL or LXL where X = any residue. These sequences are similar to the leucine-rich repeat sequences of 25-30 residues that are found in many proteins that form protein-protein interactions. More particularly in the L6 product, the leucine rich region of L6 consists of two parts with the C-terminal part of the region consisting of two direct leucine rich repeats of 146 and 149 amino acids that are 74% identical.

The above mentioned functional mutants, derivatives, parts, fragments, homologues and analogues of are referred to herein as "rust resistance-like genes" or "rust resistance genetic sequences". Reference herein to "genes" is to be taken in its broadest context and includes a classical genomic gene as well as mRNA or cDNA corresponding to the coding regions (i.e. exons) of the gene. The term "gene" is also used to describe synthetic or fusion molecules encoding all or part of a functional product. Preferred rust resistance-like genes are derived from a naturally occurring rust resistance gene by standard recombinant techniques. Generally, a rust resistance gene may be subjected to mutagenesis to produce single or multiple nucleotide substitutions, deletions and/or additions. Nucleotide insertional derivatives of the rust resistance gene of the present invention include 5′ and 3′ terminal fusions as well as intra-sequence insertions of single or multiple nucleotides. Insertional nucleotide sequence variants are those in which one or more nucleotides are introduced into a predetermined site in the nucleotide sequence although random insertion is also possible with suitable screening of the resulting product. Deletional variants are characterised by the removal of one or more nucleotides from the sequence. Substitutional nucleotide variants are those in which at least one nucleotide in the sequence has been removed and a different nucleotide inserted in its place. Such a substitution may be "silent" in that the substitution does not change the amino acid defined by the codon. Alternatively, substituents are designed to alter one amino acid for another similar acting amino acid. Typical substitutions are those made in

accordance with the following:

Suitable residues for amino acid substitutions

Original Residue	Exemplary Substitutions
Ala	Ser
Arg	Lys
Asn	Gln; His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Ala
His	Asn; Gln
Ile	Leu; Val
Leu	Ile; Val
Lys	Arg; Gln; Glu
Met	Leu; Ile
Phe	Met; Leu; Tyr
Ser	Thr
Thr	Ser
Trp	Tyr
Tyr	Trp; Phe
Val	Ile; Leu

In a particularly preferred embodiment, the rust resistance genetic sequences or like genetic sequences are employed to identify and isolate similar genes from other plants. According to this embodiment, there is contemplated a method for identifying a rust resistance genetic sequence or rust resistance-like genetic sequence in a plant, said method comprising contacting genomic DNA or cDNA isolated from said plant with a hybridisation effective amount of a genetic sequence conferring or otherwise rust resistance or part thereof and then detecting said hybridisation.

Preferably, the latter mentioned genetic sequence is from flax or similar plant such as a *Linum* species. In a most preferred embodiment, the latter genetic sequence is as set forth in SEQ ID NO:1 or corresponds to a probe such as defined in Figure 2 (SEQ ID NO:11).

Preferably, the latter genetic sequence is labelled with a reporter molecule capable of giving an identifiable signal (e.g. a radioisotope such as ^{32}P or ^{35}S or a biotintylated molecule).

Preferably, the plant to be screened is a flax, a Linum species or a grain crop plant such as wheat, barley, maize, rye, lupins or rice and/or wild varieties of same.

Alternatively, the plant is screened using antibodies to a recombinant product of a rust resistance gene. According to a first aspect of this embodiment, the present invention provides for the expression of the subject genetic sequence in a suitable host (e.g. a prokaryote or eukaryote) to produce full length or non-full length recombinant rust resistance gene products. The only requirement being that the recombinant products are immunologically interactive with antibodies to all or part of a rust resistance gene product. The immunological screening for rust resistance gene products may, in some circumstances, be more suitable than a genetic screening procedure.

Another aspect of the present invention is, therefore, directed to antibodies to a recombinant rust resistance gene product or part or fragment thereof. Such antibodies may be monoclonal or polyclonal and may be selected from naturally occurring antibodies to a rust resistance gene product or may be specifically raised to a recombinant rust resistance gene product. In the case of the latter, the rust resistance gene product may first need to be associated with a carrier molecule. Alternatively, fragments of antibodies may be used such as Fab fragments. Furthermore, the present invention extends to recombinant and synthetic antibodies and to antibody hybrids. A "synthetic antibody" is considered herein to include fragments and hybrids of antibodies. In additions, antibodies may be raised to

fragments or derivatives of the rust resistance gene product such as oligopeptides derived from or based on the product of, for example, the L6 gene. The antibodies and/or the recombinant rust resistance gene products of the present invention are particularly useful for the immunological screening of rust resistance gene products in various plants, in monitoring expression of rust resistance genetic sequences in transgenic plants and as a proprietary tagging system.

In one embodiment, specific antibodies are used to screen for rust resistance gene products in plants. Techniques for the assays contemplated herein are known in the art and include, for example, sandwich assays and ELISA.

It is within the scope of this invention to include any second antibodies (monoclonal, polyclonal or fragments of antibodies) directed to the first mentioned antibodies discussed above. Both the first and second antibodies may be used in detection assays or a first antibody may be used with a commercially available anti-immunoglobulin antibody. An antibody as contemplated herein includes any antibody specific to any region of a recombinant rust resistance gene product.

Both polyclonal and monoclonal antibodies are obtainable by immunisation with a recombinant rust resistance gene product and either type is utilisable for immunoassays. The methods of obtaining both types of sera are well known in the art. Polyclonal sera are less preferred but are relatively easily prepared by injection of a suitable laboratory animal with an effective amount of recombinant rust resistance gene product, or antigenic or immunointeractive parts thereof, collecting serum from the animal and isolating specific sera by any of the known immunoadsorbent techniques. Although antibodies produced by this method are utilisable in virtually any type of immunoassay, they are generally less favoured because of the potential heterogeneity of the product.

The use of monoclonal antibodies in an immunoassay is particularly preferred because of the ability to produce them in large quantities and the homogeneity of the product. The preparation of hybridoma cell lines for monoclonal antibody production

derived by fusing an immortal cell line and lymphocytes sensitised against the immunogenic preparation can be done by techniques which are well known to those who are skilled in the art (see, for example, references 4, 5 and 6).

The presence of a rust resistance gene product in a plant or more commonly plant extract may be accomplished in a number of ways such as by Western blotting and ELISA procedures. A wide range of immunoassay techniques are available as can be seen by reference to US Patent Nos. 4,016,043, 4, 424,279 and 4,018,653. These, of course, includes both single-site and two-site or "sandwich" assays of the non-competitive types, as well as in the traditional competitive binding assays. These assays also include direct binding of a labelled antibody to a target.

Sandwich assays are among the most useful and commonly used assays and are favoured for use in the present invention. A number of variations of the sandwich assay technique exist, and all are intended to be encompassed by the present invention. Briefly, in a typical forward assay, an unlabelled antibody is immobilised on a solid substrate and the sample to be tested brought into contact with the bound molecule. After a suitable period of incubation, for a period of time sufficient to allow formation of an antibody-antigen complex, a second antibody specific to the antigen, labelled with a reporter molecule capable of producing a detectable signal is then added and incubated, allowing time sufficient for the formation of another complex of antibody-antigen-labelled antibody. Any unreacted material is washed away, and the presence of the antigen is determined by observation of a signal produced by the reporter molecule.

In this case, the first antibody is raised to a recombinant rust resistance gene product and the antigen is a rust resistance gene product in a plant.

The results may either be qualitative, by simple observation of the visible signal, or may be quantitated by comparing with a control sample containing known amounts of hapten. Variations on the forward assay include a simultaneous assay, in which both sample and labelled antibody are added simultaneously to the bound antibody.

These techniques are well known to those skilled in the art, including any minor variations as will be readily apparent. In accordance with the present invention the sample is one which might contain rust resistance gene product and include crude or purified plant extract such as extracts of leaves, roots and stems.

In the typical forward sandwich assay, a first antibody raised against a recombinant rust resistance gene product is either covalently or passively bound to a solid surface. The solid surface is typically glass or a polymer, the most commonly used polymers being cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene. The solid supports may be in the form of tubes, beads, discs of microplates, or any other surface suitable for conducting an immunoassay. The binding processes are well-known in the art and generally consist of cross-linking, covalent binding or physically adsorption, the polymer-antibody complex is washed in preparation for the test sample. An aliquot of the sample to be tested is then added to the solid phase complex and incubated for a period of time sufficient (e.g. 2-40 minutes) and under suitable conditions (e.g. 25°C) to allow binding of any antigen present in the sample to the antibody. Following the incubation period, the reaction locus is washed and dried and incubated with a second antibody specific for a portion of the first antibody. The second antibody is linked to a reporter molecule which is used to indicate the binding of the second antibody to the hapten.

An alternative method involves immobilising the target molecules in the biological sample and then exposing the immobilised target to specific antibody which may or may not be labelled with a reporter molecule. Depending on the amount of target and the strength of the reporter molecule signal, a bound target may be detected by direct labelling with the antibody. Alternatively, a second labelled antibody, specific to the first antibody is exposed to the target-first antibody complex to form a target-first antibody-second antibody tertiary complex. The complex is detected by the signal emitted by the reporter molecule.

By "reporter molecule" as used in the present specification, is meant a molecule which, by its chemical nature, provides an analytically identifiable signal which allows the detection of antigen-bound antibody. Detection may be either qualitative or quantitative. The most commonly used reporter molecules in this type of assay are either enzymes, fluorophores or radionuclide containing molecules (i.e. radioisotopes) and chemiluminescent molecules.

In the case of an enzyme immunoassay, an enzyme is conjugated to the second antibody, generally by means of glutaraldehyde or periodate. As will be readily recognised, however, a wide variety of different conjugation techniques exist, which are readily available to the skilled artisan. Commonly used enzymes include horseradish peroxidase, glucose oxidase, beta-galactosidase and alkaline phosphatase, amongst others. The substrates to be used with the specific enzymes are generally chosen for the production, upon hydrolysis by the corresponding enzyme, of a detectable colour change. Examples of suitable enzymes include alkaline phosphatase and peroxidase. It is also possible to employ fluorogenic substrates which yield a fluorescent product rather than the chromogenic substrates noted above. In all cases, the enzyme-labelled antibody is added to the first antibody-hapten complex, allowed to bind, and then the excess reagent is washed away. A solution containing the appropriate substrate is then added to the complex of antibody-antigen-antibody. The substrate will react with the enzyme linked to the second antibody, giving a qualitative visual signal, which may be further quantitated, usually spectrophotometrically, to give an indication of the amount of hapten which was present in the sample. The term "reporter molecule" also extends to use of cell agglutination or inhibition of agglutination such as red blood cells on latex beads, and the like.

Alternately, fluorescent compounds, such as fluorescein and rhodamine, may be chemically coupled to antibodies without altering their binding capacity. When activated by illumination with light of a particular wavelength, the fluorochrome-labelled antibody adsorbs the light energy, inducing a state to excitability in the

molecule, followed by emission of the light at a characteristic colour visually detectable with a light microscope. As in enzyme immunoassays (EIA), the fluorescent labelled antibody is allowed to bind to the first antibody-hapten complex. After washing off the unbound reagent, the remaining tertiary complex is then exposed to the light of the appropriate wavelength the fluorescence observed indicates the presence of the hapten of interest. Immunofluorescene and EIA techniques are both very well established in the art and are particularly preferred for the present method. However, other reporter molecules, such as radioisotope, chemiluminescent or bioluminescent molecules, may also be employed.

It will be readily apparent to the skilled technician how to vary the above assays and all such variations are encompassed by the present invention.

The present invention is particularly described with reference to the flax rust resistance gene L and its alleles L6, L2 and L10. This is done, however, with the understanding that the subject invention extends to a range of resistance genes and alleles thereof for rust and other pathogens. In fact, the present invention extends to a resistance gene characterised by said gene encoding a product having at least one leucine rich region. Preferably, the leucine rich region is a leucine rich repeat at the 3′ end of the molecule and has at least 60% similarly to each other more preferably at least 70% similarity and even more preferably at least 80% similarity. Still more preferably, the leucine rich region corresponds to the following amino acid sequence:

PDLIELLPCELGGQTVV.VPSMAELTIRDCPRLEVGPMIRSLPKFPMLKK
LDLAVANITKEEDLDAIGSLEELVSLELELDDTSSGIERIVSSSKLQKLT
TLVVKVPSLREIEGLEELKSLQDLYLEGCTSLGRL.....PLEKLKE
LDIGGC (SEQ ID NO:12)

or having at least 60% similarly thereto or more preferably at least 70% similarity or even more preferably at least 80% similarity thereto. Alternatively or in addition to, the rust resistance gene further encodes a p-Loop at its 5′ end encoding the amino acid sequence:

GXXXXGKT/S (SEQ ID NO:8),

where X is any amino acid residue. More preferably, the p-Loop sequence comprises the amino acid residues:

GMGGIGKTT (SEQ ID NO:9),

and more particularly

GLYGMGGIGKTT (SEQ ID NO:10),

or having one or more amino acid substitutions, insertions and/or deletions thereto provided that such derivatives still function as a p-Loop. A p-Loop is involved in ATP/GTP binding. It is proposed herein that copy number and amino acid sequence of this repeated element are the determinants of the gene-for-gene specificity of rust resistance genes. Mixing and matching of these elements from existing genes will provide a potential means for creating new and useful resistance gene specificities for use in plant breeding. Such new genes are referred to herein as "modular resistance genes". This is a completely novel approach to disease resistance breeding.

According to this embodiment, there is contemplated a modular resistance gene characterised in that said gene encodes a non-naturally occurring leucine rich region. By "non-naturally occurring" is meant to include the manipulation of a genetic sequence to introduce a leucine rich encoding sequence, to increase the copy number of an existing leucine rich encoding sequence, to delete or insert a nucleotide sequence for or into a leucine rich encoding sequence or to otherwise modify a leucine rich encoding sequence to modulate pathogen specificity of a disease resistance gene. For example, the leucine rich regions of two or more of alleles of the L locus such as L6, L2 and L10 could be combined to broaden the range of pathogens to which a gene can confer resistance. Alternatively, combinations of allels from the L and M loci could be made. The present invention contemplates, therefore, a method of producing a modular resistance gene conferring resistance to a pathogen in a plant by manipulating the leucine rich regions in a disease resistance gene.

The present invention further extends to transgenic plants such as transgenic crop plants (e.g. wheat, barley or maize) carrying a non-indigenous genetic sequence conferring or otherwise facilitating rust resistance in said plant. Preferably, the non-indigenous genetic sequence is from a closely related species to the transgenic plant. The expression of the non-indigenous genetic sequence may be constitutive or inducible or developmentally regulated. Furthermore, the non-indigenous sequence may be inserted into or fused to a particular endogenous genetic sequence. In a most preferred embodiment, the transgenic plant is wheat and the non-indigenous genetic sequence is from a wild variety of wheat, barley, maize, flax or *Linum* species. Other transformed species or resistance gene sources are not excluded.

The present invention is further described by reference to the following non-limiting Figures and Examples.

In the Figures:

Figure 1 is a representation of the nucleotide sequence (SEQ ID NO:1) and corresponding amino acid sequence (SEQ ID NOs:2 to 5) of the rust resistance gene L6. There are two predicted products, the "full length" and "truncated" products. The truncated product results from an alternately spliced mRNA that retains intron 3. In the absence of the splicing of this intron, translation would continue through the 82bp intron 3 as a consequence of not changing frames, a stop codon is reached just downstream of the end of the intron. This results in a product from which the major portion of the leucine rich region is removed and also the addition of an extra 29 amino (see underlined amino acids [SEQ ID NOs: 6 and 7) that are not in the full length product.

Figure 2 is a representation of part of the L6 gene showing the LU-1 probe (underlined) and Ac insertion in mutant X75 (SEQ ID NO:11).

Figure 3 is a schematic representation of the L6 gene showing location of LU-2 probe.

Figure 4 is a representation of the amino acid sequences of the leucine rich repeat in L6.

Figure 5 is a schematic representation of the L locus alleles.

EXAMPLE 1

PLANT MATERIAL

Experiments were conducted in the line of flax called "Forge" which is homozygous for the rust resistance genes L^6, M, N and P^2 (2). One particular flax is designated TC257 and is a primary transformant of "Forge" possessing 10 copies of the maize transposable element Ac (1). Rust gene cultivars are referred to as "Birio" (L^6), "Dakota" (M), "Bombay" (N) and "Abyssinian" (P^2) (8).

EXAMPLE 2

RUST STRAINS

Four rust strains were used to screen for mutants. Three of these strains, designated CH5-78, CH5-84 and CH5-133, were obtained by selfing strain CH5. The fourth strain designated C was a parent strain of CH5. The origins of C and CH5 have been previously described (7). Each of these strains is avirulent on one of the single gene differentials and virulent on the other three. Strain CH5-84 is avirulent on "Birio" (L^6), CH5-78 is avirulent on "Dakota" (M), C is avirulent on "Bombay" (N) and CH5-133 is avirulent on "Abyssinian" (P^2). Rust maintenance and inoculation procedures were as previously described (8).

EXAMPLE 3

TRANSFORMATION

Flax cotyledons were transformed with either the vector pKU3 (9), pBT175 (10), pB135SAc11, 12 (11) or an Ac element in which the OCS enhancer (12) had been inserted at the BamH1 site at position 182, according to the protocol previously described (13).

EXAMPLE 4

TAGGING SCHEME

The tagging scheme used in this study has been described by Ellis *et al* (1) and Lawrence *et al* (13). "Forge" plants with and without Ac elements, including TC257 and its selfed progeny, were extensively crossed as the female parent with "Hoshangabad" to produce hybrid seed heterozygous for the four rust resistance genes. When seedlings were about 5cm tall, the tip was cut off and the two lateral shoots that subsequently developed were inoculated with a mixture of the four rust strains, each of which recognise a single resistance gene. Most plants were resistant to all four rust strains. Susceptible mutants were of three types, namely, "whole", in which all leaves on both lateral shoots were susceptible, "bisectored", in which all leaves on one lateral were susceptible while the other shoot was entirely resistant and "mini-sectored", in which only some of the leaves on one shoot were susceptible. When rare rust-susceptible mutants were detected, the mutant gene was identified by recovering rust spores and inoculating these on to a set of four rust resistance genes L^6, M, N or P^2. If, for example, the rust recovered from a susceptible mutant plant grew on the M, N and P^2 differentials but not on the L^6 differential, then this indicated that the plant was mutant for the L^6 gene.

EXAMPLE 5

DETECTION OF TRANSPOSED Ac ELEMENTS IN MUTANT PLANTS

The procedure for identifying transposed Ac elements was as previously described (2).

EXAMPLE 6

LAMBDA CLONING

Flax DNA was digested with *Bam*HI or *Bgl*II and the unfractionated DNA was cloned into the Lambda vector EMBL4 as previously described (3).

EXAMPLE 7

GENETIC ANALYSIS

Genetic analysis including RFLP techniques, PCR analysis, Southern blot analysis and linkage analysis were as previously described (1; 2). The nucleotide and corresponding amino acid sequence for the L6 gene is shown in Figure 1. There are two predicted products, the "full length" and "truncated" products. The truncated product results from an alternately spliced mRNA that retains intron 3. In the absence of the splicing of this intron, translation would continue through the 82bp intron 3 and as a consequence of not changing frames, a stop codon is reached just downstream of the end of the intron. This results in a product from which the major portion of the leucine rich region is removed and also the addition of an extra 29 amino acids (see underlined amino acids in Figure 1) that are not in the full length product.

EXAMPLE 8

IDENTIFICATION AND CHARACTERISATION OF A RUST-SUSCEPTIBLE MUTANT PLANT IN WHICH THE L6 GENE HAS BEEN TAGGED BY Ac

The TC257 (Example 1) line of transgenic flax containing at least 10 copies of Ac (1; 2), one of which was linked (29 map units) from the L6 rust resistance gene, was crossed extensively to a line without resistance genes and the progeny were screened for lack of L6 activity. One rust susceptible mutant lacking L6 specificity (designated mutant X75) contained a transposed Ac element which, from experimental evidence, is putatively located in the L6 gene.

EXAMPLE 9

X75 CONTAINS A TRANSPOSED AC CLOSELY LINKED TO THE MUTANT L6 GENE

The L6 mutant X75 contains a transposed Ac (referred to herein as "Tr-Ac") that is not present in its resistant parent. The location of this element was mapped with respect to the L6 gene. A joint segregation analysis of Tr-Ac and the mutant L6 gene demonstrated tight linkage of these two characters. X75 was crossed to cultivar "Birio" (L6) and progeny that inherited Tr-Ac were identified by Southern analysis. Two progeny plants, D766 and D769, were test-crossed to the cultivar "Hoshangabad" (no L6). Thirty six progeny were tested for L6 rust resistance and scored for the presence of Tr-Ac. Eighteen of the progeny were susceptible and these all possessed Tr-Ac while the remaining 18 were resistant and these all lacked Tr-Ac. This is the result expected if the allele for susceptibility is an L6 gene inactivated by Tr-Ac.

The insertion site of Tr-Ac was also mapped by restriction fragment length polymorphism (RFLP) analysis in a family of 88 test-cross progeny in which L6 was segregating. A fragment of flax DNA (probe LU-1) isolated from a lambda clone containing the 3′ junction between Tr-Ac and flax DNA, detected 3 RFLPs that distinguished the two parents when their DNA was cut with *Eco*RI, *Bgl*II and *Xba*I. The analysis of the segregation of these three markers and the L6 gene in the test-cross demonstrated that all four markers were closely linked. A single recombinant individual involving L6 and the RFLP marker detected in *Xba*I digested DNA was detected among the 88 progeny. As detailed below, this recombination event present in progeny plant D237 occurred within the region of the L6 gene.

EXAMPLE 10

RECOMBINATION IN THE VICINITY OF THE Ac INSERTION SITE ALTERS THE RESISTANCE REACTION OR SPECIFICITY OF L6

The RFLP probe LU-1 was used to establish a restriction map of the homologous regions of the resistant and susceptible parents of the test cross family and of the recombinant progeny plant D237. Three polymorphic restriction sites were detected and comparison of the maps demonstrated that a cross-over had occurred within a region of about 3kbp on either side of the Ac insertion site.

The recombinant plant D237 was selfed and 16 progeny were screened with a rust isolate that recognises L6. The progeny and were also analysed by Southern blotting to detect the recombinant chromosome. The progeny segregated for rust reaction: 6 were fully susceptible while 10 were partially resistant with restricted rust growth confined to the younger leaves. This result is consistent with the segregation of a novel gene for partial resistance which was not present in the original Forge parent. There was a complete association between the second class with novel rust reaction and the presence of the recombinant chromosome.

Thus, crossing over in the vicinity of the L6 gene results in an alteration of the L6 resistance phenotype.

EXAMPLE 11

INDEPENDENT L6 MUTANTS CONTAIN INSERTIONS IN THE REGION OF 0.5 TO 3.0KB OF THE Ac INSERTION SITE

Thirty four independent L6 mutants were isolated in the screen for tagged L6 genes. All but X75 were either deletions or, if not deletions, contained no transposed Ac elements (2). Analysis of mutants in the latter class using the LU-1 probe revealed that two of them (X3A and X117) contained a small (approximately 200bp) insertion in this region. In the case of X117, the mutant was compared to its resistant parent to confirm that the polymorphism was not pre-existing. In the case of X3A, the insertion and loss of L6 had occurred somatically. Mutant X3A arose as a sector. Among two shoots on a single F1 plant, one (X3A) had lost L6 and the second, X3B was wild-type for L6. DNA from the two sectors was examined using the LU-1 probe. An insertion was observed only in DNA from the mutant sector.

EXAMPLE 12

EXCISION OF TR-AC IN PROGENY OF X75 IS ASSOCIATED WITH REVERSION TO RUST RESISTANCE

The X75 mutant was selfed and progeny that were homozygous for the transposed Ac element were identified by Southern blotting. Selfed progeny of four such plants were in turn screened with a rust strain that recognises the L6 resistance specificity. Thirty seven resistant plants were identified among 3105 progeny. 15 of the revertants were examined by either PCR or Southern analysis for an excision fragment that would result from the excision of Ac from the L6 region. The excision marker occurred in all the plants. In two cases, the excision region was sequenced and small base changes, (an "Ac footprint") in the 8bp repeat that flanked Ac in X75 resulted from the excision process.

EXAMPLE 13

A DNA PROBE ADJACENT TO Ac DETECTS A SECOND LOCUS IN FLAX, CLOSELY LINKED TO THE M RESISTANCE LOCUS

A second DNA probe, LU-2 was isolated from the same lambda clone as LU-1. These two fragments are separated by about 2kb. LU-2, like many other flax DNA probes, hybridises to two genomic fragments in most restriction digests, providing molecular evidence for the tetraploid nature of flax. In *Xba*1 digests, LU-2 detects two polymorphic markers, LU-2-1 and LU-2-2 that distinguish the resistant and susceptible parents of a test-cross family of 52 progeny among which the L6 and M resistance genes segregate. Joint segregation analysis of these two RFLP markers and the L6 and M resistance genes demonstrated complete linkage of LU-2-1 with L6 and LU-2-2 with the resistance gene M. Thus, cloning the L6 locus has allowed access to the M resistance gene region. The LU-2 probe and A flanked Ac in X75 in L6 is shown in Figures 2 and 3.

EXAMPLE 14

RUST RESISTANCE GENES FORM A MULTIGENE FAMILY IN FLAX

The probe LU-1 and several adjacent restriction fragments from a lambda clone were used as hybridisation probes to isolate a cDNA from a library generated using leaf mRNA. A cDNA clone and several other probes from the L6 gene have been used as probes for genomic Southern analysis. These probes generally detect multiple fragments in Southern blots which indicates that flax contains a family of genes of similar sequence. All RFLPs detected with this probe map to either the L6 or M resistance gene regions.

EXAMPLE 15

PROBE LU-1 IDENTIFIES ALLELES OF L6

In genetic studies, the L locus of flax behaves as a single gene with multiple allelic specificities. Twelve resistance specificities map to the L locus. The probe LU-1 was used to examine a differential set of flax plants that each contain a single L allele (see Figures 2 and 3). DNA from the 12 differentials and from "Hoshangabad" which carries a "null" allele at the L locus was cut with *Xba*I, *Bgl*II and *Eco*RI. In each case, a single fragment was detected in the L differentials and each L allele could be distinguished from the null allele of "Hoshangabad". Using these three enzymes, 10 RFLP genotypes were detected. Only two pairs of L alleles, L3 and L4 and L6 and L7, could not be distinguished with this limited sample of digests.

EXAMPLE 16

A cDNA FROM FLAX DETECTS SEQUENCE SIMILARITY IN A WILD LINUM SPECIES

Southern analysis of DNA from the wild species, *Linum marginale* which contains genes controlling resistance against flax rust, detected strongly hybridising fragments.

EXAMPLE 17

DETERMINATION OF AMINO ACID SEQUENCE OF L6

The amino acid sequence of the L6 cDNA was determined and is shown in Figure 1. The amino acid sequence is shown in single letter code, single letter abbreviations for amino acids are defined below:

Amino Acid	One-letter Symbol
Alanine	A
Arginine	R
Asparagine	N
Aspartic acid	D
Cysteine	C
Glutamine	Q
Glutamic acid	E
Glycine	G
Histidine	H
Isoleucine	I
Leucine	L
Lysine	K
Methionine	M
Phenylalanine	F
Proline	P
Serine	S
Threonine	T
Tryptophan	W
Tyrosine	Y
Valine	V
Amino Acid	X

EXAMPLE 18

COMPARISON OF AMINO ACID SEQUENCE OF LEUCINE RICH REPEAT FROM L6

The L6 allele comprises a leucine rich repeat at amino acid residues 969 to 1115 and 1116 to 1265. This repeat was compared for identity and the comparison is shown in Figure 4. Details of the comparisons are shown below:

Length:	156 amino acids
Gaps:	3
Gap weight:	3.000
Length weight:	0.100
Quality:	160.4
Ratio:	1.091
Average match:	0.540
Average mismatch:	-0.396
Percent similarity:	82.979%
Percent identity:	74.468

EXAMPLE 19

CLONING AND COMPARISON OF L LOCUS ALLELES

Using the clones L6 gene as a probe (probe LU-1), the L2 and L10 alleles were cloned on *EcoR1* DNA fragments. These alleles have different resistance specificities and control resistance to flax rust strains that carry the AL2 and AL10 avirulence genes, respectively.

The L2 and L10 clones were subject to restriction endonuclease analysis and a schematic represented is shown in Figure 5. The L2 *EcoRI* fragment is about 400bp longer than the corresponding L10 fragment. DNA sequence analysis of both ends of the L2 and L10 fragments revealed practically identical sequence (>90%) and indicates that L2 differs from L10 by about 400bp of extra DNA. Furthermore, sequence analysis and restriction fragment mapping from internal restriction sites confirmed the extra DNA and indicated that the 5' halves of L2, L6 and L10 are very similar (>90% identical) and that the differences between the alleles occurs in the 3' half of the gene. The difference in gene length occurs in a region coding for the leucine rich repeat structure of 156 amino acids that has two copies in L6 (Figure 4)

and only one copy in a cDNA from a related but non-allelic gene called FC4.

Those skilled in the art will appreciate that the invention described herein is susceptible to variations and modifications other than those specifically described. It is to be understood that the invention includes all such variations and modifications. The invention also includes all of the steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any two or more of said steps or features.

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SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION

(ii) TITLE OF INVENTION: GENETIC SEQUENCES CONFERRING DISEASE RESISTANCE IN PLANTS AND USES THEREFOR

(iii) NUMBER OF SEQUENCES: 13

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(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25

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(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4841 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 163..789

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 1097..2203

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2669..4525

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 2293..2586

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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GAGCTCAGAA GTAAGGGATA AGGCAAGAAG CAGAGGAGCA GAGAGAAGAA CCAGCAAAGC      60

ACATGCAAAT TGAAGCAGGC AAGAACAGTT ACTGGAAATT CATTTATCTC TGCTTTCAAT     120

TTCTATCCTT CAGATCATTT CTGCTCAATT GAATCACTAG TC ATG AGT TAT TTG         174
                                                 Met Ser Tyr Leu
                                                   1

AGA GAA GTT GCT ACT GCT GTT GCC TTG CTT CTC CCT TTC ATT CTT CTC       222
Arg Glu Val Ala Thr Ala Val Ala Leu Leu Leu Pro Phe Ile Leu Leu
  5                  10                  15                  20

AAC AAG TTT TGG AGA CCA AAT TCC AAA GAC TCA ATC GTC AAC GAT GAT       270
Asn Lys Phe Trp Arg Pro Asn Ser Lys Asp Ser Ile Val Asn Asp Asp
                  25                  30                  35

GAC GAT TCA ACA TCT GAA GTT GAT GCC ATA TCC GAC TCC ACA AAT CCC       318
Asp Asp Ser Thr Ser Glu Val Asp Ala Ile Ser Asp Ser Thr Asn Pro
              40                  45                  50

TCT GGT TCA TTT CCC TCC GTG GAG TAT GAA GTG TTT TTG AGT TTC AGG       366
Ser Gly Ser Phe Pro Ser Val Glu Tyr Glu Val Phe Leu Ser Phe Arg
          55                  60                  65

GGT CCA GAT ACT CGT GAA CAG TTC ACC GAT TTC CTA TAT CAG TCT CTC       414
Gly Pro Asp Thr Arg Glu Gln Phe Thr Asp Phe Leu Tyr Gln Ser Leu
      70                  75                  80
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CGT CGC TAT AAG ATT CAC ACT TTT AGG GAC GAC GAT GAG CTA CTC AAA      462
Arg Arg Tyr Lys Ile His Thr Phe Arg Asp Asp Asp Glu Leu Leu Lys
 85                  90                  95                 100

GGA AAA GAA ATA GGG CCC AAC CTC CTA CGA GCA ATT GAT CAG TCC AAA      510
Gly Lys Glu Ile Gly Pro Asn Leu Leu Arg Ala Ile Asp Gln Ser Lys
                105                 110                 115

ATT TAC GTC CCG ATC ATA TCG AGC GGA TAT GCT GAT AGT AAG TGG TGT      558
Ile Tyr Val Pro Ile Ile Ser Ser Gly Tyr Ala Asp Ser Lys Trp Cys
            120                 125                 130

CTT ATG GAG CTT GCT GAA ATT GTG AGA CGT CAA GAG GAG GAC CCT CGA      606
Leu Met Glu Leu Ala Glu Ile Val Arg Arg Gln Glu Glu Asp Pro Arg
        135                 140                 145

CGC ATC ATA CTT CCT ATT TTT TAT ATG GTG GAT CCA AGT GAC GTA CGA      654
Arg Ile Ile Leu Pro Ile Phe Tyr Met Val Asp Pro Ser Asp Val Arg
    150                 155                 160

CAT CAG ACT GGA TGT TAT AAA AAA GCA TTT CGA AAA CAC GCA AAT AAA      702
His Gln Thr Gly Cys Tyr Lys Lys Ala Phe Arg Lys His Ala Asn Lys
165                 170                 175                 180

TTT GAT GGA CAG ACC ATA CAA AAC TGG AAA GAT GCT CTA AAG AAG GTC      750
Phe Asp Gly Gln Thr Ile Gln Asn Trp Lys Asp Ala Leu Lys Lys Val
                185                 190                 195

GGA GAC TTA AAA GGA TGG CAC ATC GGA AAG AAT GAC AAG TATGTAATCC       799
Gly Asp Leu Lys Gly Trp His Ile Gly Lys Asn Asp Lys
            200                 205

TCATCCTAGC CTTTTATCAT TCAGTACAAC TTATTTGTTT TGTCTTGCAT ATACTTACTT    859

GTTTATTGAC TAACTTTCAA ATTGCATATT AACATTCTAG GAAGATTTAA ATTGGACTCG    919

GGTCACAACT GAACCATATT ATTTTACACG ACAAAGCACG AGCTATTCCT AATGTAATTA    979

AAGTTAAAAT GCTCAATAAC GTGGAATATA TACTTGTATA CAGGGGCAAC AAACTATAAA   1039

TTGAAATATT ATTTCATATG AAGTTAACAT CTCAAAAATG TATTTAATAC TTGTAGG      1096

CAG GGA GCT ATA GCA GAC AAA GTA TCA GCA GAT ATA TGG TCA CAC ATA      1144
Gln Gly Ala Ile Ala Asp Lys Val Ser Ala Asp Ile Trp Ser His Ile
  1               5                  10                  15

AGC AAG GAA AAT CTC ATT TTA GAA ACC GAT GAG TTG GTT GGA ATT GAT      1192
Ser Lys Glu Asn Leu Ile Leu Glu Thr Asp Glu Leu Val Gly Ile Asp
            20                  25                  30

GAT CAC ATA ACA GCC GTA TTA GAA AAA TTG AGT TTA GAC TCT GAA AAT      1240
Asp His Ile Thr Ala Val Leu Glu Lys Leu Ser Leu Asp Ser Glu Asn
        35                  40                  45
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GTG ACA ATG GTC GGC CTT TAT GGT ATG GGT GGA ATA GGC AAG ACG ACC      1288
Val Thr Met Val Gly Leu Tyr Gly Met Gly Gly Ile Gly Lys Thr Thr
     50                  55                  60

ACT GCA AAG GCG GTT TAT AAC AAG ATT TCT TCT TGT TTC GAT TGT TGT      1336
Thr Ala Lys Ala Val Tyr Asn Lys Ile Ser Ser Cys Phe Asp Cys Cys
 65                  70                  75                  80

TGT TTT ATT GAC AAC ATA CGT GAA ACA CAA GAG AAG GAT GGC GTT GTT      1384
Cys Phe Ile Asp Asn Ile Arg Glu Thr Gln Glu Lys Asp Gly Val Val
                 85                  90                  95

GTT TTG CAA AAG AAG CTA GTA TCT GAA ATT TTG AGG ATC GAT TCG GGT      1432
Val Leu Gln Lys Lys Leu Val Ser Glu Ile Leu Arg Ile Asp Ser Gly
            100                 105                 110

TCG GTT GGA TTT AAT AAT GAT AGT GGC GGA CGG AAG ACG ATA AAG GAG      1480
Ser Val Gly Phe Asn Asn Asp Ser Gly Gly Arg Lys Thr Ile Lys Glu
        115                 120                 125

AGA GTT TCG AGG TTC AAA ATT CTT GTC GTT CTC GAT GAT GTG GAT GAG      1528
Arg Val Ser Arg Phe Lys Ile Leu Val Val Leu Asp Asp Val Asp Glu
    130                 135                 140

AAG TTT AAA TTT GAA GAT ATG TTG GGA AGT CCT AAA GAT TTT ATT TCT      1576
Lys Phe Lys Phe Glu Asp Met Leu Gly Ser Pro Lys Asp Phe Ile Ser
145                 150                 155                 160

CAA AGT AGA TTC ATT ATT ACT TCA AGA AGT ATG AGA GTT TTG GGT ACT      1624
Gln Ser Arg Phe Ile Ile Thr Ser Arg Ser Met Arg Val Leu Gly Thr
                165                 170                 175

TTG AAT GAG AAT CAA TGC AAG TTG TAT GAA GTT GGA TCG ATG AGC AAA      1672
Leu Asn Glu Asn Gln Cys Lys Leu Tyr Glu Val Gly Ser Met Ser Lys
            180                 185                 190

CCA CGT TCG CTT GAA CTC TTC TCC AAG CAT GCA TTC AAA AAG AAT ACG      1720
Pro Arg Ser Leu Glu Leu Phe Ser Lys His Ala Phe Lys Lys Asn Thr
        195                 200                 205

CCT CCA TCG TAT TAT GAG ACT CTA GCA AAT GAC GTC GTA GAT ACT ACA      1768
Pro Pro Ser Tyr Tyr Glu Thr Leu Ala Asn Asp Val Val Asp Thr Thr
    210                 215                 220

GCA GGA CTT CCA TTG ACT CTG AAG GTT ATA GGA TCG CTT TTA TTT AAA      1816
Ala Gly Leu Pro Leu Thr Leu Lys Val Ile Gly Ser Leu Leu Phe Lys
225                 230                 235                 240

CAA GAG ATT GCG GTT TGG GAA GAC ACG TTG GAA CAA TTA CGT AGA ACA      1864
Gln Glu Ile Ala Val Trp Glu Asp Thr Leu Glu Gln Leu Arg Arg Thr
                245                 250                 255

CTT AAC CTT GAT GAG GTT TAT GAT AGG CTA AAA ATA AGT TAT GAT GCG      1912
Leu Asn Leu Asp Glu Val Tyr Asp Arg Leu Lys Ile Ser Tyr Asp Ala
            260                 265                 270
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TTG AAC CCG GAG GCA AAA GAG ATT TTC TTG GAT ATA GCT TGC TTC TTC      1960
Leu Asn Pro Glu Ala Lys Glu Ile Phe Leu Asp Ile Ala Cys Phe Phe
        275                 280                 285

ATC GGA CAA AAT AAA GAA GAA CCG TAT TAC ATG TGG ACC GAC TGT AAT      2008
Ile Gly Gln Asn Lys Glu Glu Pro Tyr Tyr Met Trp Thr Asp Cys Asn
    290                 295                 300

TTT TAT CCA GCA AGT AAT ATT ATT TTT CTC ATT CAA AGA TGT ATG ATA      2056
Phe Tyr Pro Ala Ser Asn Ile Ile Phe Leu Ile Gln Arg Cys Met Ile
305                 310                 315                 320

CAA GTT GGG GAT GAT GAT GAG TTT AAA ATG CAC GAC CAA CTT AGA GAT      2104
Gln Val Gly Asp Asp Asp Glu Phe Lys Met His Asp Gln Leu Arg Asp
                325                 330                 335

ATG GGT AGA GAA ATT GTG AGA CGA GAG GAT GTA CTG CCG TGG AAG AGA      2152
Met Gly Arg Glu Ile Val Arg Arg Glu Asp Val Leu Pro Trp Lys Arg
            340                 345                 350

AGT AGA ATA TGG TCG GCA GAA GAA GGG ATT GAT CTC TTG CTG AAC AAA      2200
Ser Arg Ile Trp Ser Ala Glu Glu Gly Ile Asp Leu Leu Leu Asn Lys
        355                 360                 365

AAG GTATTCAGTT TTATTTAAAA TTAAATATTC ATATATTATT ACACATACTT           2253
Lys
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TAAATCACAT AACTCATTAC GTTCCTTCTC CAATTACAG GGA TCA AGT AAA GTA      2307
                                        Gly Ser Ser Lys Val
                                          1               5

AAA GCA ATT AGC ATA CCC TGG GGT GTC AAG TAT GAG TTT AAG AGC GAA      2355
Lys Ala Ile Ser Ile Pro Trp Gly Val Lys Tyr Glu Phe Lys Ser Glu
                10                  15                  20

TGT TTC TTG AAT TTG TCA GAG TTG AGA TAC CTC CAT GCA AGG GAA GCC      2403
Cys Phe Leu Asn Leu Ser Glu Leu Arg Tyr Leu His Ala Arg Glu Ala
            25                  30                  35

ATG CTT ACC GGA GAT TTC AAC AAT CTT CTC CCG AAT TTA AAG TGG CTT      2451
Met Leu Thr Gly Asp Phe Asn Asn Leu Leu Pro Asn Leu Lys Trp Leu
        40                  45                  50

GAG TTG CCA TTT TAC AAA CAT GGA GAG GAT GAT CCT CCT TTG ACC AAT      2499
Glu Leu Pro Phe Tyr Lys His Gly Glu Asp Asp Pro Pro Leu Thr Asn
    55                  60                  65

TAT ACC ATG AAA AAT CTG ATA ATT GTT ATT CTT GAG CAT AGC CAC ATA      2547
Tyr Thr Met Lys Asn Leu Ile Ile Val Ile Leu Glu His Ser His Ile
70                  75                  80                  85

ACG GCT GAT GAT TGG GGA GGT TGG AGG CAT ATG ATG AAG GTGTGTTGTT       2596
Thr Ala Asp Asp Trp Gly Gly Trp Arg His Met Met Lys
                90                  95
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TTTCAGCTGT TCATATGAAG GTGTGTTATC TTCTTATTTG TTCTTCATAT TTCTGTTTTA    2656

ATCTGCTGTC AG ATG GCT GAG AGG CTG AAA GTT GTA CGA CTT GCT TCA        2704
              Met Ala Glu Arg Leu Lys Val Val Arg Leu Ala Ser
                1               5                  10

AAC TAT AGT TTG TAC GGA AGA CGT GTT CGC CTT TCT GAC TGT TGG CGC      2752
Asn Tyr Ser Leu Tyr Gly Arg Arg Val Arg Leu Ser Asp Cys Trp Arg
         15                  20                  25

TTC CCC AAA AGC ATT GAG GTA TTA TCC ATG ACT GCG ATA GAA ATG GAT      2800
Phe Pro Lys Ser Ile Glu Val Leu Ser Met Thr Ala Ile Glu Met Asp
     30                  35                  40

GAA GTT GAT ATT GGG GAG TTA AAG AAG CTA AAG ACG TTG GTT CTG AAA      2848
Glu Val Asp Ile Gly Glu Leu Lys Lys Leu Lys Thr Leu Val Leu Lys
 45                  50                  55                  60

TTC TGT CCA ATA CAA AAG ATA AGT GGG GGA ACC TTT GGT ATG TTG AAG      2896
Phe Cys Pro Ile Gln Lys Ile Ser Gly Gly Thr Phe Gly Met Leu Lys
                 65                  70                  75

GGA CTT CGA GAG CTT TGT CTC GAA TTC AAC TGG GGG ACA AAT TTG AGA      2944
Gly Leu Arg Glu Leu Cys Leu Glu Phe Asn Trp Gly Thr Asn Leu Arg
             80                  85                  90

GAG GTA GTT GCC GAT ATT GGT CAA CTT TCA TCT CTC AAA GTC TTG AAA      2992
Glu Val Val Ala Asp Ile Gly Gln Leu Ser Ser Leu Lys Val Leu Lys
      95                  100                 105

ACA ACC GGA GCT AAG GAG GTC GAG ATT AAT GAA TTT CCA TTA GGT TTG      3040
Thr Thr Gly Ala Lys Glu Val Glu Ile Asn Glu Phe Pro Leu Gly Leu
    110                 115                 120

AAG GAG TTA TCC ACT TCA TCT CGG ATT CCG AAT CTT TCA CAG TTG TTG      3088
Lys Glu Leu Ser Thr Ser Ser Arg Ile Pro Asn Leu Ser Gln Leu Leu
125                 130                 135                 140

GAT TTG GAG GTA CTG AAG GTT TAT GAT TGC AAG GAT GGA TTT GAC ATG      3136
Asp Leu Glu Val Leu Lys Val Tyr Asp Cys Lys Asp Gly Phe Asp Met
                145                 150                 155

CCT CCT GCT AGT CCG AGT GAA GAT GAA AGT AGT GTG TGG TGG AAG GTA      3184
Pro Pro Ala Ser Pro Ser Glu Asp Glu Ser Ser Val Trp Trp Lys Val
            160                 165                 170

TCC AAG TTG AAG TCT TTG CAA CTC GAG AAG ACA AGA ATC AAT GTC AAC      3232
Ser Lys Leu Lys Ser Leu Gln Leu Glu Lys Thr Arg Ile Asn Val Asn
        175                 180                 185

GTT GTG GAT GAT GCT TCT TCC GGT GGT CAC CTC CCT CGT TAC TTA CTA      3280
Val Val Asp Asp Ala Ser Ser Gly Gly His Leu Pro Arg Tyr Leu Leu
    190                 195                 200
```

```
CCA ACA TCC CTA ACC TAT CTT AAA ATT TAT CAG TGT ACA GAA CCA ACG      3328
Pro Thr Ser Leu Thr Tyr Leu Lys Ile Tyr Gln Cys Thr Glu Pro Thr
205                 210                 215                 220

TGG CTT CCA GGA ATA GAG AAC TTG GAG AAT TTG ACT TCG CTG GAA GTC      3376
Trp Leu Pro Gly Ile Glu Asn Leu Glu Asn Leu Thr Ser Leu Glu Val
                225                 230                 235

AAC GAC ATC TTC CAA ACT CTT GGA GGT GAC TTG GAT GGG CTA CAA GGG      3424
Asn Asp Ile Phe Gln Thr Leu Gly Gly Asp Leu Asp Gly Leu Gln Gly
            240                 245                 250

TTG AGA TCA TTG GAA ATT CTT AGG ATT CGG AAA GTA AAT GGT TTA GCT      3472
Leu Arg Ser Leu Glu Ile Leu Arg Ile Arg Lys Val Asn Gly Leu Ala
        255                 260                 265

CGG ATC AAA GGG CTT AAG GAT CTC TTG TGT TCT TCT ACC TGC AAG TTG      3520
Arg Ile Lys Gly Leu Lys Asp Leu Leu Cys Ser Ser Thr Cys Lys Leu
    270                 275                 280

CGG AAA TTT TAT ATT ACA GAA TGC CCC GAC CTC ATT GAG TTA CTC CCA      3568
Arg Lys Phe Tyr Ile Thr Glu Cys Pro Asp Leu Ile Glu Leu Leu Pro
285                 290                 295                 300

TGC GAA CTC GGC GGC CAA ACA GTA GTA GTC CCC TCT ATG GCA GAA CTG      3616
Cys Glu Leu Gly Gly Gln Thr Val Val Val Pro Ser Met Ala Glu Leu
                305                 310                 315

ACC ATT AGG GAT TGT CCA CGG CTG GAG GTT GGC CCG ATG ATA AGA TCA      3664
Thr Ile Arg Asp Cys Pro Arg Leu Glu Val Gly Pro Met Ile Arg Ser
            320                 325                 330

CTC CCA AAG TTC CCA ATG CTA AAG AAG TTG GAC CTC GCG GTG GCA AAT      3712
Leu Pro Lys Phe Pro Met Leu Lys Lys Leu Asp Leu Ala Val Ala Asn
        335                 340                 345

ATA ACT AAA GAG GAG GAT CTG GAT GCG ATT GGA TCC CTA GAA GAG TTG      3760
Ile Thr Lys Glu Glu Asp Leu Asp Ala Ile Gly Ser Leu Glu Glu Leu
    350                 355                 360

GTT AGT TTG GAG TTA GAG TTA GAC GAT ACA TCT TCC GGT ATA GAG AGG      3808
Val Ser Leu Glu Leu Glu Leu Asp Asp Thr Ser Ser Gly Ile Glu Arg
365                 370                 375                 380

ATA GTT TCC TCT TCG AAG CTG CAA AAG TTA ACT ACA CTC GTA GTG AAG      3856
Ile Val Ser Ser Ser Lys Leu Gln Lys Leu Thr Thr Leu Val Val Lys
                385                 390                 395

GTG CCG AGT TTG CGG GAG ATT GAA GGG CTT GAA GAG TTG AAG TCT TTA      3904
Val Pro Ser Leu Arg Glu Ile Glu Gly Leu Glu Glu Leu Lys Ser Leu
            400                 405                 410

CAA GAT TTG TAT CTA GAG GGT TGC ACG TCG TTG GGG AGA CTA CCA CTG      3952
Gln Asp Leu Tyr Leu Glu Gly Cys Thr Ser Leu Gly Arg Leu Pro Leu
        415                 420                 425
```

```
GAG AAG CTG AAG GAG CTA GAC ATT GGA GGA TGC CCT GAC CTC ACT GAG      4000
Glu Lys Leu Lys Glu Leu Asp Ile Gly Gly Cys Pro Asp Leu Thr Glu
    430                 435                 440

TTA GTC CAA ACA GTA GTA GCA GTC CCC TCT TTG AGA GGA CTG ACC ATT      4048
Leu Val Gln Thr Val Val Ala Val Pro Ser Leu Arg Gly Leu Thr Ile
445                 450                 455                 460

AGG GAT TGT CCA CGG CTG GAG GTT GGT CCA ATG ATA CAA TCT CTT CCA      4096
Arg Asp Cys Pro Arg Leu Glu Val Gly Pro Met Ile Gln Ser Leu Pro
                465                 470                 475

AAG TTC CCA ATG CTA AAT GAA TTG ACG CTC TCG ATG GTA AAT ATC ACT      4144
Lys Phe Pro Met Leu Asn Glu Leu Thr Leu Ser Met Val Asn Ile Thr
            480                 485                 490

AAG GAG GAT GAG CTG GAG GTG CTT GGA TCC CTA GAA GAG TTG GAT AGT      4192
Lys Glu Asp Glu Leu Glu Val Leu Gly Ser Leu Glu Glu Leu Asp Ser
        495                 500                 505

TTG GAG TTA ACG TTA GAC GAT ACA TGT TCC AGC ATA GAG AGG ATA TCT      4240
Leu Glu Leu Thr Leu Asp Asp Thr Cys Ser Ser Ile Glu Arg Ile Ser
    510                 515                 520

TTC TTG TCG AAG CTG CAA AAG TTA ACT ACA CTC ATA GTG GAG GTG CCG      4288
Phe Leu Ser Lys Leu Gln Lys Leu Thr Thr Leu Ile Val Glu Val Pro
525                 530                 535                 540

AGT TTG CGG GAG ATT GAA GGT CTT GCA GAG TTG AAG TCT TTA CGA ATT      4336
Ser Leu Arg Glu Ile Glu Gly Leu Ala Glu Leu Lys Ser Leu Arg Ile
                545                 550                 555

TTG TAT CTA GAA GGA TGC ACG TCG TTG GAA AGA CTG TGG CCT GAT CAA      4384
Leu Tyr Leu Glu Gly Cys Thr Ser Leu Glu Arg Leu Trp Pro Asp Gln
            560                 565                 570

CAA CAG TTG GGT AGT CTG AAG AAC CTG AAT GTG CTC GAC ATC CAA GGT      4432
Gln Gln Leu Gly Ser Leu Lys Asn Leu Asn Val Leu Asp Ile Gln Gly
        575                 580                 585

TGT AAA AGC TTG AGT GTT GAC CAT CTC TCT GCA CTC AAG ACC ACT CTA      4480
Cys Lys Ser Leu Ser Val Asp His Leu Ser Ala Leu Lys Thr Thr Leu
    590                 595                 600

CCG CCC AGG GCG AGG ATA ACA TGG CCC GAT CAG CCC TAC AGA TGACGGTAGG   4532
Pro Pro Arg Ala Arg Ile Thr Trp Pro Asp Gln Pro Tyr Arg
605                 610                 615

AATTAATGCA AGTGACAGTG ATGACATAGT TGTGATGGCT TGCACCTGAT CAACCTTGTT   4592

CTTCATGGGG TTTTCTCCCC AGTGAGATCT TAATATCCAA AATTCTGGTT TGTTCAGAGG   4652

TTATATGGTT CAGTTTTTCA CCATAATATT TTCTACGGCA TAGCGCAAAC TACTTCTAGT   4712

ATATAGATAT AGGCAATATA TATAACATCC AACTCTGTTT TACTCACTCC TCTCATCTTC   4772
```

TCACTCGATT ATGTTCCATT TCTAAAATCC ATTATTCATC GCCTTATATT CATAATTATG 4832

TAATTATTT 4841

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 208 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Ser Tyr Leu Arg Glu Val Ala Thr Ala Val Ala Leu Leu Leu Pro
1 5 10 15

Phe Ile Leu Leu Asn Lys Phe Trp Arg Pro Asn Ser Lys Asp Ser Ile
20 25 30

Val Asn Asp Asp Asp Asp Ser Thr Ser Glu Val Asp Ala Ile Ser Asp
35 40 45

Ser Thr Asn Pro Ser Gly Ser Phe Pro Ser Val Glu Tyr Glu Val Phe
50 55 60

Leu Ser Phe Arg Gly Pro Asp Thr Arg Glu Gln Phe Thr Asp Phe Leu
65 70 75 80

Tyr Gln Ser Leu Arg Arg Tyr Lys Ile His Thr Phe Arg Asp Asp Asp
85 90 95

Glu Leu Leu Lys Gly Lys Glu Ile Gly Pro Asn Leu Leu Arg Ala Ile
100 105 110

Asp Gln Ser Lys Ile Tyr Val Pro Ile Ile Ser Ser Gly Tyr Ala Asp
115 120 125

Ser Lys Trp Cys Leu Met Glu Leu Ala Glu Ile Val Arg Arg Gln Glu
130 135 140

Glu Asp Pro Arg Arg Ile Ile Leu Pro Ile Phe Tyr Met Val Asp Pro
145 150 155 160

Ser Asp Val Arg His Gln Thr Gly Cys Tyr Lys Lys Ala Phe Arg Lys
165 170 175

His Ala Asn Lys Phe Asp Gly Gln Thr Ile Gln Asn Trp Lys Asp Ala
180 185 190

```
Leu Lys Lys Val Gly Asp Leu Lys Gly Trp His Ile Gly Lys Asn Asp
        195                 200                 205

Lys
```

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 369 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

```
Gln Gly Ala Ile Ala Asp Lys Val Ser Ala Asp Ile Trp Ser His Ile
  1               5                  10                  15

Ser Lys Glu Asn Leu Ile Leu Glu Thr Asp Glu Leu Val Gly Ile Asp
             20                  25                  30

Asp His Ile Thr Ala Val Leu Glu Lys Leu Ser Leu Asp Ser Glu Asn
         35                  40                  45

Val Thr Met Val Gly Leu Tyr Gly Met Gly Gly Ile Gly Lys Thr Thr
     50                  55                  60

Thr Ala Lys Ala Val Tyr Asn Lys Ile Ser Ser Cys Phe Asp Cys Cys
 65                  70                  75                  80

Cys Phe Ile Asp Asn Ile Arg Glu Thr Gln Glu Lys Asp Gly Val Val
                 85                  90                  95

Val Leu Gln Lys Lys Leu Val Ser Glu Ile Leu Arg Ile Asp Ser Gly
            100                 105                 110

Ser Val Gly Phe Asn Asn Asp Ser Gly Gly Arg Lys Thr Ile Lys Glu
        115                 120                 125

Arg Val Ser Arg Phe Lys Ile Leu Val Val Leu Asp Asp Val Asp Glu
    130                 135                 140

Lys Phe Lys Phe Glu Asp Met Leu Gly Ser Pro Lys Asp Phe Ile Ser
145                 150                 155                 160

Gln Ser Arg Phe Ile Ile Thr Ser Arg Ser Met Arg Val Leu Gly Thr
                165                 170                 175

Leu Asn Glu Asn Gln Cys Lys Leu Tyr Glu Val Gly Ser Met Ser Lys
            180                 185                 190
```

```
Pro Arg Ser Leu Glu Leu Phe Ser Lys His Ala Phe Lys Lys Asn Thr
        195                 200                 205

Pro Pro Ser Tyr Tyr Glu Thr Leu Ala Asn Asp Val Val Asp Thr Thr
    210                 215                 220

Ala Gly Leu Pro Leu Thr Leu Lys Val Ile Gly Ser Leu Leu Phe Lys
225                 230                 235                 240

Gln Glu Ile Ala Val Trp Glu Asp Thr Leu Glu Gln Leu Arg Arg Thr
                245                 250                 255

Leu Asn Leu Asp Glu Val Tyr Asp Arg Leu Lys Ile Ser Tyr Asp Ala
            260                 265                 270

Leu Asn Pro Glu Ala Lys Glu Ile Phe Leu Asp Ile Ala Cys Phe Phe
        275                 280                 285

Ile Gly Gln Asn Lys Glu Glu Pro Tyr Tyr Met Trp Thr Asp Cys Asn
    290                 295                 300

Phe Tyr Pro Ala Ser Asn Ile Ile Phe Leu Ile Gln Arg Cys Met Ile
305                 310                 315                 320

Gln Val Gly Asp Asp Asp Glu Phe Lys Met His Asp Gln Leu Arg Asp
                325                 330                 335

Met Gly Arg Glu Ile Val Arg Arg Glu Asp Val Leu Pro Trp Lys Arg
            340                 345                 350

Ser Arg Ile Trp Ser Ala Glu Glu Gly Ile Asp Leu Leu Leu Asn Lys
        355                 360                 365

Lys
```

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 98 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```
Gly Ser Ser Lys Val Lys Ala Ile Ser Ile Pro Trp Gly Val Lys Tyr
  1               5                  10                  15

Glu Phe Lys Ser Glu Cys Phe Leu Asn Leu Ser Glu Leu Arg Tyr Leu
            20                  25                  30
```

```
His Ala Arg Glu Ala Met Leu Thr Gly Asp Phe Asn Asn Leu Leu Pro
         35                  40                  45

Asn Leu Lys Trp Leu Glu Leu Pro Phe Tyr Lys His Gly Glu Asp Asp
     50                  55                  60

Pro Pro Leu Thr Asn Tyr Thr Met Lys Asn Leu Ile Ile Val Ile Leu
 65                  70                  75                  80

Glu His Ser His Ile Thr Ala Asp Asp Trp Gly Gly Trp Arg His Met
                 85                  90                  95

Met Lys
```

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 619 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

```
Met Ala Glu Arg Leu Lys Val Val Arg Leu Ala Ser Asn Tyr Ser Leu
 1               5                  10                  15

Tyr Gly Arg Arg Val Arg Leu Ser Asp Cys Trp Arg Phe Pro Lys Ser
            20                  25                  30

Ile Glu Val Leu Ser Met Thr Ala Ile Glu Met Asp Glu Val Asp Ile
        35                  40                  45

Gly Glu Leu Lys Lys Leu Lys Thr Leu Val Leu Lys Phe Cys Pro Ile
    50                  55                  60

Gln Lys Ile Ser Gly Gly Thr Phe Gly Met Leu Lys Gly Leu Arg Glu
65                  70                  75                  80

Leu Cys Leu Glu Phe Asn Trp Gly Thr Asn Leu Arg Glu Val Val Ala
                85                  90                  95

Asp Ile Gly Gln Leu Ser Ser Leu Lys Val Leu Lys Thr Thr Gly Ala
            100                 105                 110

Lys Glu Val Glu Ile Asn Glu Phe Pro Leu Gly Leu Lys Glu Leu Ser
        115                 120                 125

Thr Ser Ser Arg Ile Pro Asn Leu Ser Gln Leu Leu Asp Leu Glu Val
    130                 135                 140

Leu Lys Val Tyr Asp Cys Lys Asp Gly Phe Asp Met Pro Pro Ala Ser
145                 150                 155                 160
```

Pro Ser Glu Asp Glu Ser Ser Val Trp Trp Lys Val Ser Lys Leu Lys
165 170 175

Ser Leu Gln Leu Glu Lys Thr Arg Ile Asn Val Asn Val Val Asp Asp
180 185 190

Ala Ser Ser Gly Gly His Leu Pro Arg Tyr Leu Leu Pro Thr Ser Leu
195 200 205

Thr Tyr Leu Lys Ile Tyr Gln Cys Thr Glu Pro Thr Trp Leu Pro Gly
210 215 220

Ile Glu Asn Leu Glu Asn Leu Thr Ser Leu Glu Val Asn Asp Ile Phe
225 230 235 240

Gln Thr Leu Gly Gly Asp Leu Asp Gly Leu Gln Gly Leu Arg Ser Leu
245 250 255

Glu Ile Leu Arg Ile Arg Lys Val Asn Gly Leu Ala Arg Ile Lys Gly
260 265 270

Leu Lys Asp Leu Leu Cys Ser Ser Thr Cys Lys Leu Arg Lys Phe Tyr
275 280 285

Ile Thr Glu Cys Pro Asp Leu Ile Glu Leu Leu Pro Cys Glu Leu Gly
290 295 300

Gly Gln Thr Val Val Val Pro Ser Met Ala Glu Leu Thr Ile Arg Asp
305 310 315 320

Cys Pro Arg Leu Glu Val Gly Pro Met Ile Arg Ser Leu Pro Lys Phe
325 330 335

Pro Met Leu Lys Lys Leu Asp Leu Ala Val Ala Asn Ile Thr Lys Glu
340 345 350

Glu Asp Leu Asp Ala Ile Gly Ser Leu Glu Glu Leu Val Ser Leu Glu
355 360 365

Leu Glu Leu Asp Asp Thr Ser Ser Gly Ile Glu Arg Ile Val Ser Ser
370 375 380

Ser Lys Leu Gln Lys Leu Thr Thr Leu Val Val Lys Val Pro Ser Leu
385 390 395 400

Arg Glu Ile Glu Gly Leu Glu Glu Leu Lys Ser Leu Gln Asp Leu Tyr
405 410 415

Leu Glu Gly Cys Thr Ser Leu Gly Arg Leu Pro Leu Glu Lys Leu Lys
420 425 430

Glu Leu Asp Ile Gly Gly Cys Pro Asp Leu Thr Glu Leu Val Gln Thr
435 440 445

```
Val Val Ala Val Pro Ser Leu Arg Gly Leu Thr Ile Arg Asp Cys Pro
    450                 455                 460

Arg Leu Glu Val Gly Pro Met Ile Gln Ser Leu Pro Lys Phe Pro Met
465                 470                 475                 480

Leu Asn Glu Leu Thr Leu Ser Met Val Asn Ile Thr Lys Glu Asp Glu
                485                 490                 495

Leu Glu Val Leu Gly Ser Leu Glu Glu Leu Asp Ser Leu Glu Leu Thr
            500                 505                 510

Leu Asp Asp Thr Cys Ser Ser Ile Glu Arg Ile Ser Phe Leu Ser Lys
        515                 520                 525

Leu Gln Lys Leu Thr Thr Leu Ile Val Glu Val Pro Ser Leu Arg Glu
    530                 535                 540

Ile Glu Gly Leu Ala Glu Leu Lys Ser Leu Arg Ile Leu Tyr Leu Glu
545                 550                 555                 560

Gly Cys Thr Ser Leu Glu Arg Leu Trp Pro Asp Gln Gln Gln Leu Gly
                565                 570                 575

Ser Leu Lys Asn Leu Asn Val Leu Asp Ile Gln Gly Cys Lys Ser Leu
            580                 585                 590

Ser Val Asp His Leu Ser Ala Leu Lys Thr Thr Leu Pro Pro Arg Ala
        595                 600                 605

Arg Ile Thr Trp Pro Asp Gln Pro Tyr Arg
    610                 615
```

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 90 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 1..90

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

```
GTG TGT TGT TTT TCA GCT GTT CAT ATG AAG GTG TGT TAT CTT CTT ATT      48
Val Cys Cys Phe Ser Ala Val His Met Lys Val Cys Tyr Leu Leu Ile
 1               5                  10                  15

TGT TCT TCA TAT TTC TGT TTT AAT CTG CTG TCA GAT GGC TG              90
Cys Ser Ser Tyr Phe Cys Phe Asn Leu Leu Ser Asp Gly
            20                  25                  30
```

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

```
Val Cys Cys Phe Ser Ala Val His Met Lys Val Cys Tyr Leu Leu Ile
 1               5                  10                  15

Cys Ser Ser Tyr Phe Cys Phe Asn Leu Leu Ser Asp Gly
            20                  25
```

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

(xi(i)) /: Alternative amino acid

Gly Xaa Xaa Xaa Xaa Gly Lys Thr / Ser
1 5

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Gly Met Gly Gly Ile Gly Lys Thr Thr
1 5

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Gly Leu Tyr Gly Met Gly Gly Ile Gly Lys Thr Thr
1 5 10

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 840 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

AAAAAAAAAT TATAAGTTAA CAATTATACG TATGTTCCTA ACAATTGCTA AATAAATATT 60

ATCTCATCCT TCACTCCATT TTAGCAATTG TTAAAATTTT GGAATCGATA AATCTCGATC 120

CACTAACCAC TTCAAAATAG AAAAATAATG CGTAGCACAC AAACAACAGG ATTGGTGGCC 180

CCTTGATCAT GTAGCCAATT AGGTGATTCT TGTGGACAAG TAGAACTAGT TGTACTCGCT 240

AACCGGTCCG ATTTGAAATT TGACCCAGGT TTCGAAATTC TAACCAACCC AAATGGTTGA 300

CTGACTTGTG GGCCTGCATT ATTTGTAGAT AAGAAAGAGT TTACAAATGG TTGGCTTACA 360

TTGAATTTGT GGAGCAATAA TTGAGTTTTT GAATGGAGGA TACTGAAAGC CAGTGGGAGC 420

TCAGAAGTAA GGGATAAGGC AAGAAGCAGA GGAGCAGAGA GAAGAACCAG CAAAGCACAT 480

GCAAATTGAA GCAGGCAAGA ACAGTTACTG GAAATTCATT TATCTCTGCT TTCAATTTCT 540

ATCCTTCAGA TCATTTCTGC TCAATTGAAT CACTAGTCAT GAGTTATTTG AGAGAAGTTG 600

CTACTGCTGT TGCCTTGCTT CTCCCTTTCA TTCTTCTCAA CAAGTTTTGG AGACCAAATT 660

CCAAAGACTC AATCGTCAAC GATGATGACG ATTCAACATC TGAAGTTGAT GCCATATCCG 720

ACTCCACAAA TCCCTCTGGT TCATTTCCCT CCGTGGAGTA TGAAGTGTTT TTGAGTTTCA 780

GGGGTCCAGA TACTCGTGAA CAGTTCACCG ATTTCCTATA TCAGTCTCTC CGTCGCTATA 840

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 150 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

```
Pro Asp Leu Thr Glu Leu Val Gln Thr Val Val Ala Val Pro Ser Leu
1               5                  10                  15

Arg Gly Leu Thr Ile Arg Asp Cys Pro Arg Leu Glu Val Gly Pro Met
            20                  25                  30

Ile Gln Ser Leu Pro Lys Phe Pro Met Leu Asn Glu Leu Thr Leu Ser
        35                  40                  45

Met Val Asn Ile Thr Lys Glu Asp Glu Leu Glu Val Leu Gly Ser Leu
    50                  55                  60

Glu Glu Leu Asp Ser Leu Glu Leu Thr Leu Asp Asp Thr Cys Ser Ser
65                  70                  75                  80

Ile Glu Arg Ile Ser Phe Leu Ser Lys Leu Gln Lys Leu Thr Thr Leu
                85                  90                  95

Ile Val Glu Val Pro Ser Leu Arg Glu Ile Glu Gly Leu Ala Glu Leu
            100                 105                 110

Lys Ser Leu Arg Ile Leu Tyr Leu Glu Gly Cys Thr Ser Leu Glu Arg
        115                 120                 125

Leu Trp Pro Asp Gln Gln Gln Leu Gly Ser Leu Lys Asn Leu Asn Val
    130                 135                 140

Leu Asp Ile Gln Gly Cys
145                 150
```

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

Ile Leu Val Val Leu Asp Asp Val Asp
1 5

CLAIMS

1. An isolated nucleic acid molecule comprising a sequence of nucleotides which confers or otherwise facilitates disease resistance in plants.

2. An isolated nucleic acid molecule according to claim 1 wherein the disease resistance is rust resistance.

3. An isolated nucleic aid molecule according to claim 2 comprising a sequence of nucleotides as set forth in SEQ ID NO:1 or having at least 45% similarity to all or part thereof.

4. An isolated nucleic acid molecule according to claim 2 comprising a sequence of nucleotides encoding or complementary to a sequence of nucleotides encoding the amino acid sequence set forth in SEQ ID NOs:2 to 5 or having at least 45% similarity to all or part thereof.

5. An isolated nucleic acid molecule comprising a sequence of nucleotides encoding or complementary to a sequence encoding a peptide, polypeptide or protein which is capable of interacting with an avirulence gene product on a flax rust.

6. An isolated nucleic acid molecule according to claim 5 wherein the nucleic acid molecule corresponds to an allele of rust resistance gene L or M.

7. An isolated nucleic acid molecule according to claim 5 or 6 wherein the nucleic acid molecule corresponds to an L6 allele of rust resistance gene L and the corresponding avirulence gene is AL6.

8. An isolated nucleic acid molecule according to claim 5 or 6 wherein the nucleic acid molecule corresponds to the L2 allele of the rust resistance gene L and the corresponding avirulence gene is AL2.

9. An isolated nucleic acid molecule according to claim 5 or 6 wherein the nucleic acid molecule corresponds to the L10 allele of the rust resistance gene L and the corresponding avirulence gene is AL10.

10. An isolated nucleic acid molecule which:

(i) confers rust resistance in a plant; and

(ii) is capable of hybridizing under low stringency conditions to the nucleic acid molecule defined in SEQ ID NO:1.

11. An isolated nucleic acid molecule according to claim 10 wherein the nucleic acid molecule is capable of hybridizing to the nucleic acid defined in SEQ ID NOs:2 to 5 under medium stringent conditions.

12. An isolated nucleic acid molecule according to claim 10 wherein the nucleic acid molecule is capable to hybridizing to the nucleic acid defined in SEQ ID NO:11 under high stringent conditions.

13. An isolated nucleic acid molecule according to claim 10 or 11 or 12 having a nucleotide sequence substantially corresponding to the nucleotide sequence set forth in SEQ ID NO:1 or having at least 80% similarity to all or part thereof.

14. An isolated nucleic acid molecule according to claim 1 or 5 or 10 isolatable from a flax plant.

15. An isolated nucleic acid molecule according to claim 1 or 5 or 10 isolatable from a species of *Linum* or a soybean, sunflower, cereal, or wild varieties of wheat or barley.

16. An isolated nucleic acid molecule according to claim 15 isolatable from *Linum marginale.*

17. A method for identifying a rust resistance genetic sequence in a plant, said method comprising contacting genomic DNA or cDNA or mRNA from said plant with a hybridizing effective amount of a genetic sequence conferring or facilitating rust resistance or part thereof and then detecting said hybridization.

18. A method according to claim 17 wherein the plant is flax.

19. A method according to claim 17 wherein the plant is a species of *Linum*, soybean, sunflower, cereal, or a wild variety of wheat or barley.

20. A method according to claim 17 wherein the plant is *Linum marginale*.

21. A method according to claim 17 wherein the rust resistance genetic sequence is as set forth in SEQ ID NO:1 or is a portion or part thereof encoding rust resistance or has at least 60% similarity thereto.

22. A method according to claim 17 wherein the rust resistance genetic sequence encodes an amino acid sequence substantially as set forth in SEQ ID NOs:2 to 5 or having at least 60% similarity thereto.

23. An isolated nucleic acid molecule comprising a sequence of nucleotides which:

(i) confers or otherwise facilitates disease resistance in plants; and

(ii) encodes a product having at least one leucine rich region and/or comprises a p-loop at the 5' end of the nucleic acid molecule which encodes the amino acid sequence:

GXXXXGKT/S,

where X is any amino acid residue.

24. An isolated nucleic acid molecule according to claim 23 wherein the leucine rich region is a leucine rich repeat encoded by the 3' end of the molecule.

25. A nucleic acid molecule according to claim 23 or 24 wherein the leucine region comprises the amino acid sequence:

PDLIELLPCELGGQTVV.VPSMAELTIRDCPRLEVGPMIRSLPKFPMLKK
LDLAVANITKEEDLDAIGSLEELVSLELELDDTSSGIERIVSSSKLQKLT
TLVVKVPSLREIEGLEELKSLQDLYLEGCTSLGRL.....PLEKLKE
LDIGGC

or having at least 60% similarity to all or part thereof.

26. A nucleic acid molecule according to claim 23 wherein the p-loop sequence encodes the amino acid residues:

GMGGIGKTT

27. A nucleic acid molecule according to claim 23 wherein the p-loop sequence encodes the amino acid residues:

GLYGMGGIGKTT

28. A nucleic acid molecule according to claim 23 wherein the disease resistance is rust resistance.

29. A nucleic acid molecule according to claim 28 wherein the plant is a crop plant.

30. A nucleic acid molecule according to claim 29 wherein the plant is wheat or barley.

31. A nucleic acid molecule according to claim 23 comprising a nucleotide sequence as set forth in SEQ ID NO:1 or encoding an amino acid sequence as set forth in SEQ ID NOs:2 to 5 or having at least 60% similarity to all or part thereof.

32. A modular resistance gene comprising heterologous genetic sequences from at least two nucleic acid molecules encoding disease resistance in plants.

33. A modular resistance gene according to claim 32 wherein the disease resistance is rust resistance.

34. A modular resistance gene according to claim 33 comprising all or part of genetic sequences encoding leucine rich regions from alleles of at least two rust resistance genes selected from L and M.

35. A modular resistance gene according to claim 34 comprising all or part of genetic sequences encoding leucine rich regions from alleles of at least two rust resistance genes selected from L6, L2 and L10.

36. A transgenic plant carrying a non-indigenous genetic sequence conferring or otherwise facilitating rust resistance in said plant.

37. A transgenic plant according to claim 36 wherein the non-indigenous sequence comprises all or part of the nucleotide sequence set forth in SEQ ID NO:1 or encodes an amino acid sequence as set forth in SEQ ID NOs:2 to 5 or having at least 60% similarity to all or part thereof.

38. A transgenic plant according to claim 36 or 37 wherein said plant is wheat or barley.

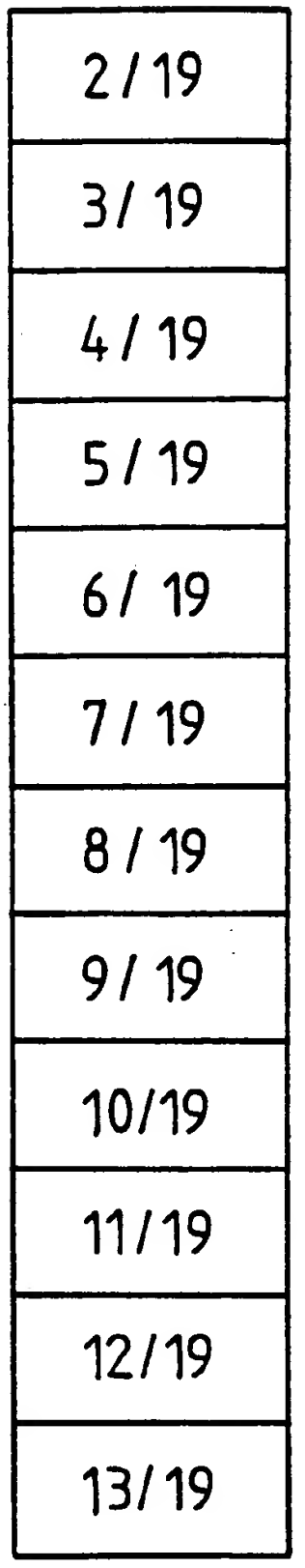

FIG 1

FIGURE 1

a.a.		nt.
	GAGCTCAGAAGTAAGGGATAAGGCAAGAAGCAGAGGAGCAGAGAGAAGAACCAGCAAAGC	60
	ACATGCAAATTGAAGCAGGCAAGAACAGTTACTGGAAATTCATTTATCTCTGCTTTCAAT	120
	TTCTATCCTTCAGATCATTTCTGCTCAATTGAATCACTAGTCATGAGTTATTTGAGAGAA	180
1	M S Y L R E	
	GTTGCTACTGCTGTTGCCTTGCTTCTCCCTTTCATTCTTCTCAACAAGTTTTGGAGACCA	240
7	V A T A V A L L L P F I L L N K F W R P	
	AATTCCAAAGACTCAATCGTCAACGATGATGACGATTCAACATCTGAAGTTGATGCCATA	300
27	N S K D S I V N D D D D S T S E V D A I	
	TCCGACTCCACAAATCCCTCTGGTTCATTTCCCTCCGTGGAGTATGAAGTGTTTTTGAGT	360
47	S D S T N P S G S F P S V E Y E V F L S	
	TTCAGGGGTCCAGATACTCGTGAACAGTTCACCGATTTCCTATATCAGTCTCTCCGTCGC	420
67	F R G P D T R E Q F T D F L Y Q S L R R	
	TATAAGATTCACACTTTTAGGGACGACGATGAGCTACTCAAAGGAAAAGAAATAGGGCCC	480

FIGURE 1

```
 87   Y  K  I  H  T  F  R  D  D  D  E  L  L  K  G  K  E  I  G  P
      AACCTCCTACGAGCAATTGATCAGTCCAAAATTTACGTCCCGATCATATCGAGCGGATAT  540

107   N  L  L  R  A  I  D  Q  S  K  I  Y  V  P  I  I  S  S  G  Y
      GCTGATAGTAAGTGGTGTCTTATGGAGCTTGCTGAAATTGTGAGACGTCAAGAGGAGGAC  600

127   A  D  S  K  W  C  L  M  E  L  A  E  I  V  R  R  Q  E  E  D
      CCTCGACGCATCATACTTCCTATTTTTTATATGGTGGATCCAAGTGACGTACGACATCAG   660

147   P  R  R  I  I  L  P  I  F  Y  M  V  D  P  S  D  V  R  H  Q
      ACTGGATGTTATAAAAAAGCATTTCGAAAACACGCAAATAAATTTGATGGACAGACCATA  720

167   T  G  C  Y  K  K  A  F  R  K  H  A  N  K  F  D  G  Q  T  I
      CAAAACTGGAAAGATGCTCTAAAGAAGGTCGGAGACTTAAAAGGATGGCACATCGGAAAG  780

187   Q  N  W  K  D  A  L  K  K  V  G  D  L  K  G  W  H  I  G  K
      AATGACAAGTATGTAATCCTCATCCTAGCCTTTTATCATTCAGTACAACTTATTTGTTTT  840

207   N  D  K
      GTCTTGCATATACTTACTTGTTTATTGACTAACTTTCAAATTGCATATTAACATTCTAGG  900
```

FIGURE 1

```
          AAGATTTAAATTGGACTCGGGTCACAACTGAACCATATTATTTTACACGACAAAGCACGA  960

          GCTATTCCTAATGTAATTAAAGTTAAAATGCTCAATAACGTGGAATATATACTTGTATAC 1020

          AGGGGCAACAAACTATAAATTGAAATATTATTTCATATGAAGTTAACATCTCAAAAATGT 1080

          ATTTAATACTTGTAGGCAGGGAGCTATAGCAGACAAAGTATCAGCAGATATATGGTCACA 1140

210                         Q  G  A  I  A  D  K  V  S  A  D  I  W  S  H
          CATAAGCAAGGAAAATCTCATTTTAGAAACCGATGAGTTGGTTGGAATTGATGATCACAT 1200

225        I  S  K  E  N  L  I  L  E  T  D  E  L  V  G  I  D  D  H  I
          AACAGCCGTATTAGAAAAATTGAGTTTAGACTCTGAAAATGTGACAATGGTCGGCCTTTA 1260

245        T  A  V  L  E  K  L  S  L  D  S  E  N  V  T  M  V  G  L  Y
          TGGTATGGGTGGAATAGGCAAGACGACCACTGCAAAGGCGGTTTATAACAAGATTTCTTC 1320

265        G  M  G  G  I  G  K  T  T  T  A  K  A  V  Y  N  K  I  S  S
          TTGTTTCGATTGTTGTTGTTTTATTGACAACATACGTGAAACACAAGAGAAGGATGGCGT 1380

285        C  F  D  C  C  C  F  I  D  N  I  R  E  T  Q  E  K  D  G  V
```

FIGURE 1

```
                TGTTGTTTTGCAAAAGAAGCTAGTATCTGAAATTTTGAGGATCGATTCGGGTTCGGTTGG  1440

305              V  V  L  Q  K  K  L  V  S  E  I  L  R  I  D  S  G  S  V  G
                 ATTTAATAATGATAGTGGCGGACGGAAGACGATAAAGGAGAGAGTTTCGAGGTTCAAAAT  1500

325              F  N  N  D  S  G  G  R  K  T  I  K  E  R  V  S  R  F  K  I
                 TCTTGTCGTTCTCGATGATGTGGATGAGAAGTTTAAATTTGAAGATATGTTGGGAAGTCC  1560

345              L  V  V  L  D  D  V  D  E  K  F  K  F  E  D  M  L  G  S  P
                 TAAAGATTTTATTTCTCAAAGTAGATTCATTATTACTTCAAGAAGTATGAGAGTTTTGGG  1620

365              K  D  F  I  S  Q  S  R  F  I  I  T  S  R  S  M  R  V  L  G
                 TACTTTGAATGAGAATCAATGCAAGTTGTATGAAGTTGGATCGATGAGCAAACCACGTTC  1680

385              T  L  N  E  N  Q  C  K  L  Y  E  V  G  S  M  S  K  P  R  S
                 GCTTGAACTCTTCTCCAAGCATGCATTCAAAAAGAATACGCCTCCATCGTATTATGAGAC  1740

405              L  E  L  F  S  K  H  A  F  K  K  N  T  P  P  S  Y  Y  E  T
                 TCTAGCAAATGACGTCGTAGATACTACAGCAGGACTTCCATTGACTCTGAAGGTTATAGG  1800

425              L  A  N  D  V  V  D  T  T  A  G  L  P  L  T  L  K  V  I  G
```

FIGURE 1

```
        ATCGCTTTTATTTAAACAAGAGATTGCGGTTTGGGAAGACACGTTGGAACAATTACGTAG   1860

445      S  L  L  F  K  Q  E  I  A  V  W  E  D  T  L  E  Q  L  R  R
        AACACTTAACCTTGATGAGGTTTATGATAGGCTAAAAATAAGTTATGATGCGTTGAACCC   1920

465      T  L  N  L  D  E  V  Y  D  R  L  K  I  S  Y  D  A  L  N  P
        GGAGGCAAAAGAGATTTTCTTGGATATAGCTTGCTTCTTCATCGGACAAAATAAAGAAGA   1980

485      E  A  K  E  I  F  L  D  I  A  C  F  F  I  G  Q  N  K  E  E
        ACCGTATTACATGTGGACCGACTGTAATTTTTATCCAGCAAGTAATATTATTTTTCTCAT   2040

505      P  Y  Y  M  W  T  D  C  N  F  Y  P  A  S  N  I  I  F  L  I
        TCAAAGATGTATGATACAAGTTGGGGATGATGATGAGTTTAAAATGCACGACCAACTTAG   2100

525      Q  R  C  M  I  Q  V  G  D  D  D  E  F  K  M  H  D  Q  L  R
        AGATATGGGTAGAGAAATTGTGAGACGAGAGGATGTACTGCCGTGGAAGAGAAGTAGAAT   2160

545      D  M  G  R  E  I  V  R  R  E  D  V  L  P  W  K  R  S  R  I
        ATGGTCGGCAGAAGAAGGGATTGATCTCTTGCTGAACAAAAAGGTATTCAGTTTTATTTA   2220

565      W  S  A  E  E  G  I  D  L  L  L  N  K  K
```

FIGURE 1

```
        AAATTAAATATTCATATATTATTACACATACTTTAAATCACATAACTCATTACGTTCCTT   2280

        CTCCAATTACAGGGATCAAGTAAAGTAAAAGCAATTAGCATACCCTGGGGTGTCAAGTAT   2340

579                   G  S  S  K  V  K  A  I  S  I  P  W  G  V  K  Y
        GAGTTTAAGAGCGAATGTTTCTTGAATTTGTCAGAGTTGAGATACCTCCATGCAAGGGAA   2400

595     E  F  K  S  E  C  F  L  N  L  S  E  L  R  Y  L  H  A  R  E
        GCCATGCTTACCGGAGATTTCAACAATCTTCTCCCGAATTTAAAGTGGCTTGAGTTGCCA   2460

615     A  M  L  T  G  D  F  N  N  L  L  P  N  L  K  W  L  E  L  P
        TTTTACAAACATGGAGAGGATGATCCTCCTTTGACCAATTATACCATGAAAAATCTGATA   2520

635     F  Y  K  H  G  E  D  D  P  P  L  T  N  Y  T  M  K  N  L  I
        ATTGTTATTCTTGAGCATAGCCACATAACGGCTGATGATTGGGGAGGTTGGAGGCATATG   2580

655     I  V  I  L  E  H  S  H  I  T  A  D  D  W  G  G  W  R  H  M
        ATGAAGGTGTGTTGTTTTTCAGCTGTTCATATGAAGGTGTGTTATCTTCTTATTTGTTCT   2640
```

FIGURE 1

675 M K [v c c f s a v h m k v c y l l i c s

TCATATTTCTGTTTTAATCTGCTGTCAGATGGCTGAGAGGCTGAAAGTTGTACGACTTGC 2700

s y f c f n l l s d g *l

677 M A E R L K V V R L A

TTCAAACTATAGTTTGTACGGAAGACGTGTTCGCCTTTCTGACTGTTGGCGCTTCCCCAA 2760

688 S N Y S L Y G R R V R L S D C W R F P K

AAGCATTGAGGTATTATCCATGACTGCGATAGAAATGGATGAAGTTGATATTGGGGAGTT 2820

708 S I E V L S M T A I E M D E V D I G E L

AAAGAAGCTAAAGACGTTGGTTCTGAAATTCTGTCCAATACAAAAGATAAGTGGGGGAAC 2880

728 K K L K T L V L K F C P I Q K I S G G T

CTTTGGTATGTTGAAGGGACTTCGAGAGCTTTGTCTCGAATTCAACTGGGGGACAAATTT 2940

748 F G M L K G L R E L C L E F N W G T N L

GAGAGAGGTAGTTGCCGATATTGGTCAACTTTCATCTCTCAAAGTCTTGAAAACAACCGG 3000

FIGURE 1

```
768    R  E  V  V  A  D  I  G  Q  L  S  S  L  K  V  L  K  T  T  G
       AGCTAAGGAGGTCGAGATTAATGAATTTCCATTAGGTTTGAAGGAGTTATCCACTTCATC   3060

788    A  K  E  V  E  I  N  E  F  P  L  G  L  K  E  L  S  T  S  S
       TCGGATTCCGAATCTTTCACAGTTGTTGGATTTGGAGGTACTGAAGGTTTATGATTGCAA   3120

808    R  I  P  N  L  S  Q  L  L  D  L  E  V  L  K  V  Y  D  C  K
       GGATGGATTTGACATGCCTCCTGCTAGTCCGAGTGAAGATGAAAGTAGTGTGTGGTGGAA   3180

828    D  G  F  D  M  P  P  A  S  P  S  E  D  E  S  S  V  W  W  K
       GGTATCCAAGTTGAAGTCTTTGCAACTCGAGAAGACAAGAATCAATGTCAACGTTGTGGA   3240

848    V  S  K  L  K  S  L  Q  L  E  K  T  R  I  N  V  N  V  V  D
       TGATGCTTCTTCCGGTGGTCACCTCCCTCGTTACTTACTACCAACATCCCTAACCTATCT   3300

868    D  A  S  S  G  G  H  L  P  R  Y  L  L  P  T  S  L  T  Y  L
       TAAAATTTATCAGTGTACAGAACCAACGTGGCTTCCAGGAATAGAGAACTTGGAGAATTT   3360

888    K  I  Y  Q  C  T  E  P  T  W  L  P  G  I  E  N  L  E  N  L
       GACTTCGCTGGAAGTCAACGACATCTTCCAAACTCTTGGAGGTGACTTGGATGGGCTACA   3420
```

FIGURE 1

```
908    T  S  L  E  V  N  D  I  F  Q  T  L  G  G  D  L  D  G  L  Q
       AGGGTTGAGATCATTGGAAATTCTTAGGATTCGGAAAGTAAATGGTTTAGCTCGGATCAA   3480

928    G  L  R  S  L  E  I  L  R  I  R  K  V  N  G  L  A  R  I  K
       AGGGCTTAAGGATCTCTTGTGTTCTTCTACCTGCAAGTTGCGGAAATTTTATATTACAGA   3540

948    G  L  K  D  L  L  C  S  S  T  C  K  L  R  K  F  Y  I  T  E
       ATGCCCCGACCTCATTGAGTTACTCCCATGCGAACTCGGCGGCCAAACAGTAGTAGTCCC   3600

968    C  P  D  L  I  E  L  L  P  C  E  L  G  G  Q  T  V  V  V  P
       CTCTATGGCAGAACTGACCATTAGGGATTGTCCACGGCTGGAGGTTGGCCCGATGATAAG   3660

988    S  M  A  E  L  T  I  R  D  C  P  R  L  E  V  G  P  M  I  R
       ATCACTCCCAAAGTTCCCAATGCTAAAGAAGTTGGACCTCGCGGTGGCAAATATAACTAA   3720

1008   S  L  P  K  F  P  M  L  K  K  L  D  L  A  V  A  N  I  T  K
       AGAGGAGGATCTGGATGCGATTGGATCCCTAGAAGAGTTGGTTAGTTTGGAGTTAGAGTT   3780

1028   E  E  D  L  D  A  I  G  S  L  E  E  L  V  S  L  E  L  E  L
       AGACGATACATCTTCCGGTATAGAGAGGATAGTTTCCTCTTCGAAGCTGCAAAAGTTAAC   3840
```

FIGURE 1

```
1048    D  D  T  S  S  G  I  E  R  I  V  S  S  S  K  L  Q  K  L  T
        TACACTCGTAGTGAAGGTGCCGAGTTTGCGGGAGATTGAAGGGCTTGAAGAGTTGAAGTC  3900

1068    T  L  V  V  K  V  P  S  L  R  E  I  E  G  L  E  E  L  K  S
        TTTACAAGATTTGTATCTAGAGGGTTGCACGTCGTTGGGGAGACTACCACTGGAGAAGCT  3960

1088    L  Q  D  L  Y  L  E  G  C  T  S  L  G  R  L  P  L  E  K  L
        GAAGGAGCTAGACATTGGAGGATGCCCTGACCTCACTGAGTTAGTCCAAACAGTAGTAGC  4020

1108    K  E  L  D  I  G  G  C  P  D  L  T  E  L  V  Q  T  V  V  A
        AGTCCCCTCTTTGAGAGGACTGACCATTAGGGATTGTCCACGGCTGGAGGTTGGTCCAAT  4080

1128    V  P  S  L  R  G  L  T  I  R  D  C  P  R  L  E  V  G  P  M
        GATACAATCTCTTCCAAAGTTCCCAATGCTAAATGAATTGACGCTCTCGATGGTAAATAT  4140

1148    I  Q  S  L  P  K  F  P  M  L  N  E  L  T  L  S  M  V  N  I
        CACTAAGGAGGATGAGCTGGAGGTGCTTGGATCCCTAGAAGAGTTGGATAGTTTGGAGTT  4200

1168    T  K  E  D  E  L  E  V  L  G  S  L  E  E  L  D  S  L  E  L
        AACGTTAGACGATACATGTTCCAGCATAGAGAGGATATCTTTCTTGTCGAAGCTGCAAAA  4260
```


PCT/AU95/00240

FIGURE 1

```
1188    T  L  D  D  T  C  S  S  I  E  R  I  S  F  L  S  K  L  Q  K
        GTTAACTACACTCATAGTGGAGGTGCCGAGTTTGCGGGAGATTGAAGGTCTTGCAGAGTT  4320

1208    L  T  T  L  I  V  E  V  P  S  L  R  E  I  E  G  L  A  E  L
        GAAGTCTTTACGAATTTTGTATCTAGAAGGATGCACGTCGTTGGAAAGACTGTGGCCTGA  4380

1228    K  S  L  R  I  L  Y  L  E  G  C  T  S  L  E  R  L  W  P  D
        TCAACAACAGTTGGGTAGTCTGAAGAACCTGAATGTGCTCGACATCCAAGGTTGTAAAAG  4440

1248    Q  Q  Q  L  G  S  L  K  N  L  N  V  L  D  I  Q  G  C  K  S
        CTTGAGTGTTGACCATCTCTCTGCACTCAAGACCACTCTACCGCCCAGGGCGAGGATAAC  4500

1268    L  S  V  D  H  L  S  A  L  K  T  T  L  P  P  R  A  R  I  T
        ATGGCCCGATCAGCCCTACAGATGACGGTAGGAATTAATGCAAGTGACAGTGATGACATA  4560

1288    W  P  D  Q  P  Y  R  *
        GTTGTGATGGCTTGCACCTGATCAACCTTGTTCTTCATGGGGTTTTCTCCCCAGTGAGAT  4620

        CTTAATATCCAAAATTCTGGTTTGTTCAGAGGTTATATGGTTCAGTTTTTCACCATAATA  4680

        TTTTCTACGGCATAGCGCAAACTACTTCTAGTATATAGATATAGGCAATATATATAACAT  4740
```

FIGURE 1

CCAACTCTGTTTTACTCACTCCTCTCATCTTCTCACTCGATTATGTTCCATTTCTAAAAT 4800

CCATTATTCATCGCCTTATATTCATAATTATGTAATTATTT 4838

FIG 2

FIGURE 2

↓ HincII

AAAAAAAAAT TATAAGTTAA CAATTATACG TATGTTCCTA ACAATTGCTA AATAAATATT 60

ATCTCATCCT TCACTCCATT TTAGCAATTG TTAAAATTTT GGAATCGATA AATCTCGATC 120

CACTAACCAC TTCAAAATAG AAAAATAATG CGTAGCACAC AAACAACAGG ATTGGTGGCC 180

CCTTGATCAT GTAGCCAATT AGGTGATTCT TGTGGACAAG TAGAACTAGT TGTACTCGCT 240

↓ HincII

AACCGGTCCG ATTTGAAATT TGACCCAGGT TTCGAAATTC TAACCAACCC AAATGGTTGA 300

CTGACTTGTG GGCCTGCATT ATTTGTAGAT AAGAAAGAGT TTACAAATGG TTGGCTTACA 360

TTGAATTTGT GGAGCAATAA TTGAGTTTTT GAATGGAGGA TACTGAAAGC CAGTGGGAGC 420

TCAGAAGTAA GGGATAAGGC AAGAAGCAGA GGAGCAGAGA GAAGAACCAG CAAAGCACAT 480

GCAAATTGAA GCAGGCAAGA ACAGTTACTG GAAATTCATT TATCTCTGCT TTCAATTTCT 540

ATCCTTCAGA TCATTTCTGC TCAATTGAAT CACTAGTCAT GAGTTATTTG AGAGAAGTTG 600

FIGURE 2

```
CTACTGCTGT TGCCTTGCTT CTCCCTTTCA TTCTTCTCAA CAAGTTTTGG AGACCAAATT      660
                  ↓ HincII
CCAAAGACTC AATCGTCAAC GATGATGACG ATTCAACATC TGAAGTTGAT GCCATATCCG      720
                                          ↓ Ac insertion in X75 mutant
ACTCCACAAA TCCCTCTGGT TCATTTCCCT CCGTGGAGTA TGAAGTGTTT TTGAGTTTCA      780

GGGGTCCAGA TACTCGTGAA CAGTTCACCG ATTTCCTATA TCAGTCTCTC CGTCGCTATA      840
```

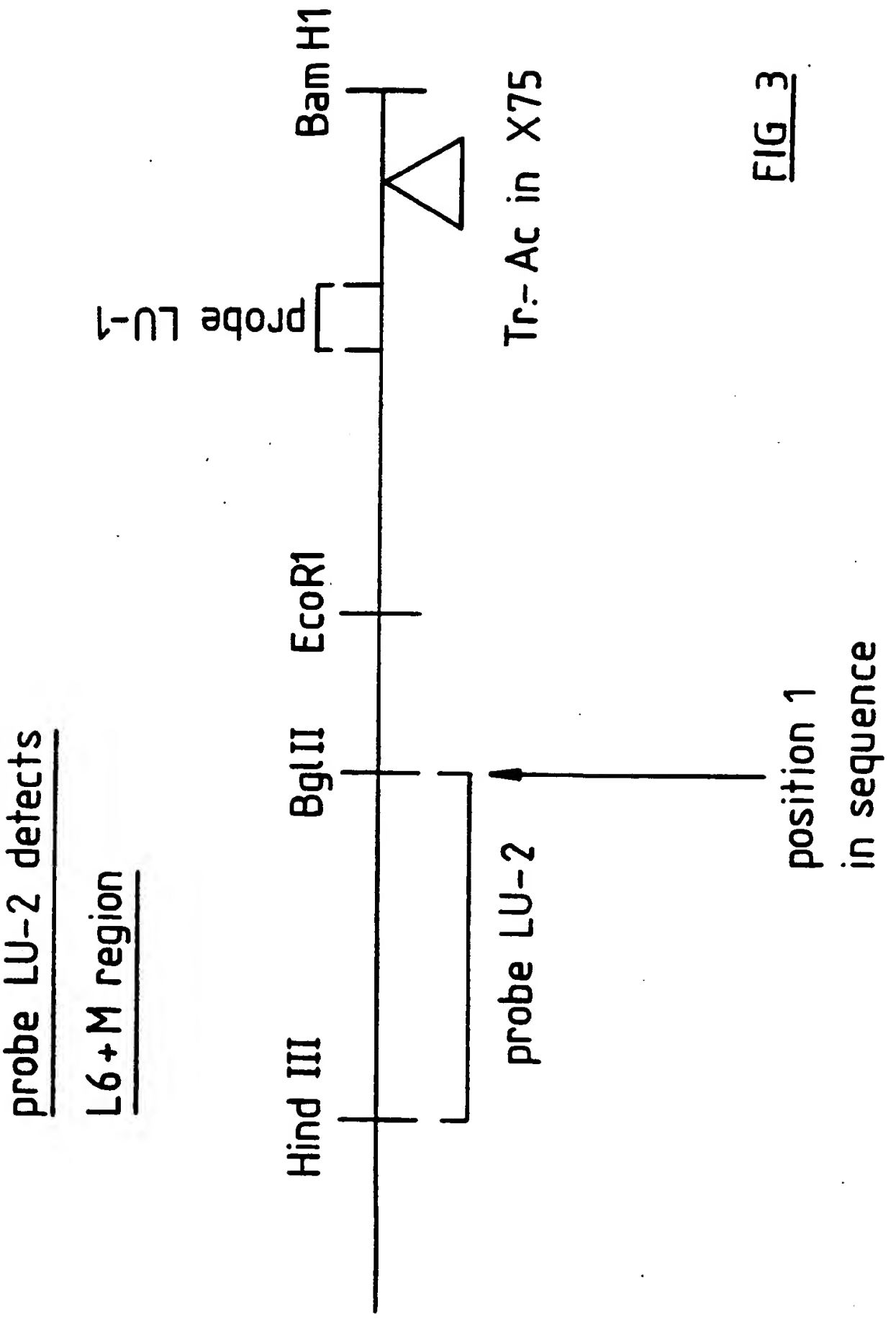
Bam H1
Tr.- Ac in X75
probe LU-1
coR1
Eco
BglII
position 1
in sequence
probe LU-2
Hind III
probe LU-2 detects
L6+M region

FIG 3

FIGURE 4

```
969  PDLIELLPCELGGQTVV.VPSMAELTIRDCPRLEVGPMIRSLPKFPMLKK 1017
     |||.||:      ||||  |||: :|||||||||||||||.||||||||..
1116 PDLTELV......QTVVAVPSLRGLTIRDCPRLEVGPMIQSLPKFPMLNE 1159

1018 LDLAVANITKEEDLDAIGSLEELVSLELELDDTSSGIERIVSSSKLQKLT 1067
     |.|.:.|||||:|:|:.:|||||| ||||.||||:|:||||   |||||||
1160 LTLSMVNITKEDELEVLGSLEELDSLELTLDDTCSSIERISFLSKLQKLT 1209

1068 TLVVKVPSLREIEGLEELKSLQDLYLEGCTSLGRL.....PLEKLKE 1109
     ||:|.||||||||||.|||||. ||||||||||:||        .|..|.
1210 TLIVEVPSLREIEGLAELKSLRILYLEGCTSLERLWPDQQQLGSLKNLNV 1259

1110 LDIGGC 1115
     |||.||
1260 LDIQGC 1265
```

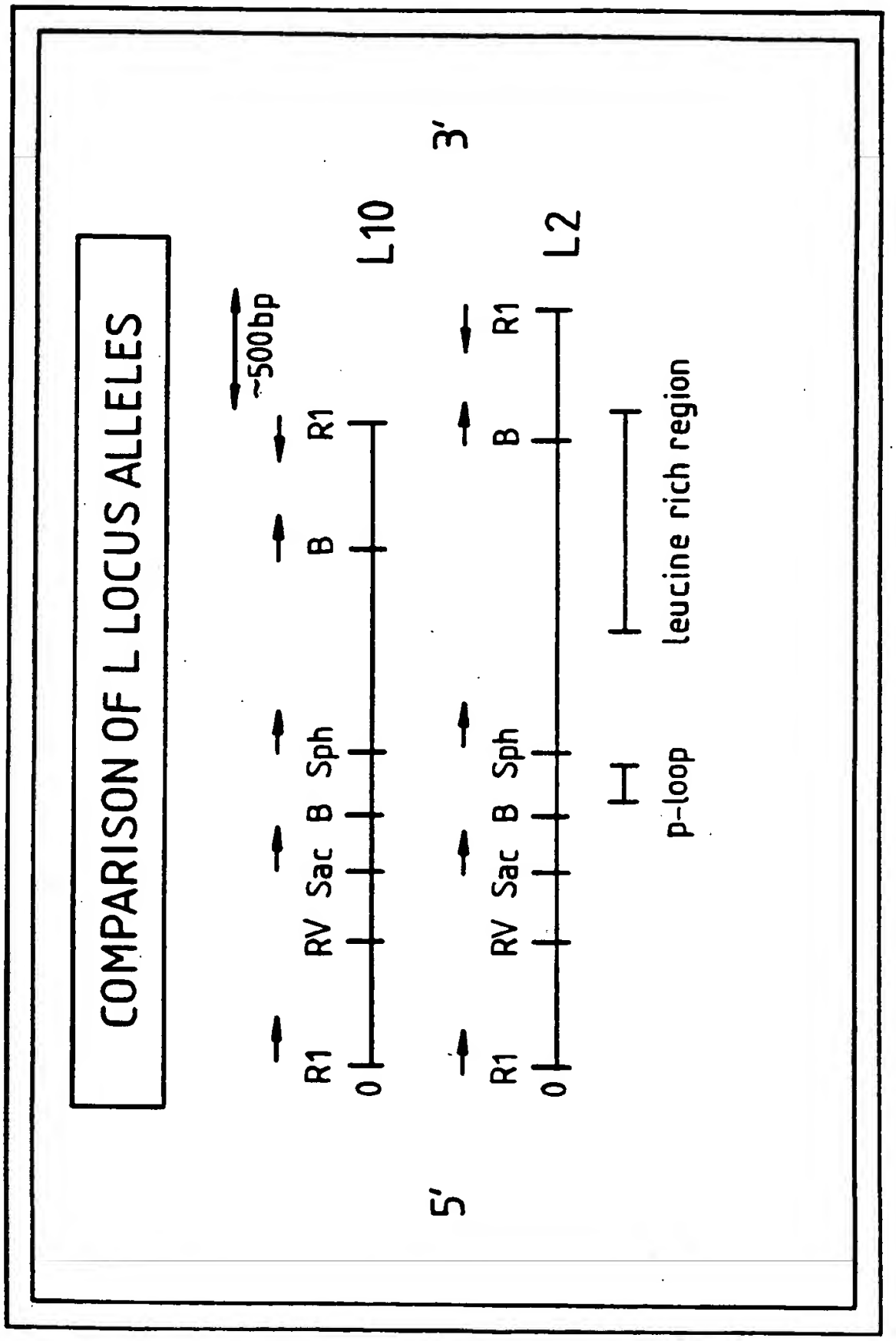
COMPARISON OF L LOCUS ALLELES
3'
L10
L2
~500bp
R1
B
R1
B
R1
RV Sac B Sph
R1
RV Sac B Sph
0
0
leucine rich region
p-loop
5'

FIG 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU 95/00240

A. CLASSIFICATION OF SUBJECT MATTER
Int. Cl.[6] C12N 15/29; C12Q 1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
WPAT : CASM : Keywords as below

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base, and where practicable, search terms used)
WPAT : rust and C12N/IC or A01H/IC or C07K/IC
CASM (1) : rust and gene: or DNA or nucleic acid: and resist: or protect: or avirulen: and plant and 1990-1995 (2) leucine rich and plant: and 1990-1995 and resist: or protect: or avirulen: (3) plant: and p(w) loop or leucine (s) rich
BIOSIS : (1) search 1 above (years 1985-1995) (2) search 3 above
STN search : GXXXXGKT; GXXXXGKS; GMGGIGKTT; GLEELKSL; GLYGMGGIGKTT; TTCGA and 1989-1995 and rust and resist:

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
P,X	Science vol. 265 pages 1856-1860 (23 September 1994) A.F. Bent et al "RPS2 of Arabidopsis thaliana: A Leucine-Rich Repeat Class of Plant Disease Resistance Genes" (see whole document, in particular, column 2 page 1858 and figure 4)	1, 23

[X] Further documents are listed in the continuation of Box C.

[ ] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 August 1995	11 AUGUST 1995 (11.08.95)
Name and mailing address of the ISA/AU AUSTRALIAN INDUSTRIAL PROPERTY ORGANISATION PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No. 06 2853929	Authorized officer for Arati Sardesai KAREN AYERS Telephone No. (06) 2832082

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate of the relevant passages	Relevant to Claim No.
P,X	Science, vol. 266 pages 789-793 (4 November 1994) P.A. Jones et al "Isolation of the tomato Cf.9 Gene for Resistance to Cladosporium fulvum by Transposon Tagging" (see whole document, in particular columns 2 and 3, page 791)	1
P,X	Cell, volume 78, pages 1101-1115 (September 23, 1994), S. Whitham et al "The Product of the Tobacco Mosaic Virus Resistance Gene N: Similarity to toll and the Interleukin-1 receptor (see whole document)	1
X Y	Bio/Technology volume 11 (9) (September 1993) pages 1048-1052, E. Truve et al "Transgenic potato plants expressing Mammalian 2'-5' oligoadenylate synthetase are protected from potato virus X Infection under field conditions " (see whole document)	1 32
X Y	Science, volume 258 (November 6, 1992) pages 985-987, G.S. Johal and S.P. Briggs, "Reductase activity encoded by the HM1 Disease Resistance Gene in Maize" (see whole document)	1 32
X Y	Science, volume 262 (November 26, 1993) pages 1432-1436, G.B. Martin et al "Map-Based cloning of a protein kinase gene conferring Disease resistance in Tomato" (see whole document)	1 32
A	Advances in Molecular Genetics of Plant-Microbe Interactions, volume 14 (1993), pages 469-475, A. Pryor "Transposon tagging of a rust resistance gene in maize" (see whole document)	1-38
A	Advances in Molecular Genetics of Plant-Microbe Interactions, volume 14 (1993), pages 511-515, H.J. Newbury et al "Mutagenesis of a race-specific rust resistance gene in Antirrhinum Majus using a transposon-tagging protocol" (see whole document)	1-38
T	Cell, volume 80 (February 10, 1995), pages 363-366, J.L. Dangl, "Pièce de Rèsistance: Novel Classes of Plant Disease Resistance Genes". (See whole document, particularly columns 2 and 2, page 363)	1-38